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Screening for Depression, Anxiety, and Suicide Risk in Children and Adolescents: An Evidence Review for the U.S. Preventive Services Task Force

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Structured Abstract

Purpose: To review the evidence on screening (benefits and harms of screening, accuracy of screening, benefits and harms of treatment) for suicide risk, anxiety, and depression in children and adolescents in settings relevant to primary care in the United States for the U.S. Preventive Services Task Force.

Data Sources: PubMed, the Cochrane Library, PsycINFO, CINAHL and trial registries through July 19, 2021; bibliographies from retrieved articles, outside experts, and surveillance of the literature through June 1, 2022.

Study Selection: Two investigators independently selected English-language studies using a priori defined criteria. We included trials that evaluated the benefits or harms of screening for suicide risk, anxiety, or depression compared with no screening or usual care. We included studies of screening with instruments feasible in primary care settings. For treatment benefits and harms, we included drugs approved for pediatric use by the Food and Drug Administration. For suicide and depression treatment studies, we included any eligible psychotherapy or collaborative care interventions. For anxiety, we restricted nonpharmacological interventions to cognitive behavioral therapy (CBT). Eligible outcomes included test accuracy, symptoms, response, remission, loss of diagnosis, all-cause mortality, functioning, suicide-related symptoms or events, withdrawal due to adverse events, serious adverse events, and harms from screening. We also included systematic reviews reporting on harms of treatment. We excluded studies with poor methodological quality.

Data Extraction and Analysis: One investigator extracted data and a second checked accuracy. Two reviewers independently rated methodological quality for all included studies. When at least three similar studies were available, we conducted meta-analyses.

Data Synthesis: We included 80 studies (in 106 publications). No studies evaluated the direct benefits of screening compared with no screening or usual care. Seventeen studies reported on accuracy of screening instruments for one or more conditions; of these, one reported on suicide (N=580), 10 on anxiety (N=3,260), seven on depression (N=3,316), and two on anxiety or depression (N=695). Studies reported a wide range for sensitivity and specificity across a variety of instruments, with no more than one or two studies on each instrument. For suicide, sensitivity ranged from 0.87 to 0.91, and specificity was 0.60. For anxiety, sensitivity generally ranged from 0.34 to 1.00, and specificity from 0.47 to 0.98. For depression, sensitivity ranged from 0.59 to 0.94, and specificity from 0.38 to 0.96. Two RCTs (N=2,675) compared short-term distress from screening for suicide risk and reported no significant differences between those screened and those who were not screened.

Sixty randomized, controlled trials (RCTs) addressed benefits of treatment; of these, 16 reported on suicide risk interventions (N=3,034), 29 on anxiety treatment (N=2,970), 13 on depression treatment (N=2,156), and two on depression or anxiety treatment (N=236). Interventions addressing suicide risk or self-harm reported lower scores for the Beck Hopelessness Scale (pooled mean difference: -2.35 [95% confidence interval [CI], -4.06 to -0.65]; N=644; k=4) for

intervention arms when compared with control arms. Findings for other measures were mixed or not statistically significantly different.

Of the 29 RCTs on anxiety treatment, 22 were on CBT; six were on pharmacotherapy; and one had multiple arms evaluating CBT, sertraline, and CBT plus sertraline. The evidence suggests CBT was associated with gains on several pooled measures of symptom improvement (magnitude of change varies by outcome measure), response (pooled relative risk [RR]: 1.89 [95% CI, 1.17 to 3.05]; N=606; k=6; I2=64%), remission (RR: 2.68 [95% CI, 1.48 to 4.88]; N=321; k=4), and loss of diagnosis (RRs range from 3.02 to 3.09), when compared with usual care or wait-list. The evidence on functioning for CBT was mixed. The evidence suggests pharmacotherapy, when compared with placebo, was associated with gains on two pooled measures of symptom improvement (mean difference Pediatric Anxiety Rating Scale: -4.0 [95% CI, -5.5 to -2.5], N=726, k=5 and mean difference Clinical Global Impressions-Severity: -0.84 [95% CI, -1.13 to -0.55]; N=550, k=4) and response (RR: 2.11 [95% CI, 1.58 to 2.98]; N=370; k=5) but was mixed on measures of functioning.

Of the 13 RCTs on depression treatment, eight were on psychotherapy; two on pharmacotherapy; one on CBT, fluoxetine, and their combination; and one on collaborative care. Results for psychotherapy varied by measure. Two pooled estimates suggested that psychotherapy is associated with improved symptoms (Beck Depression Inventory [BDI] or BDI-II standardized mean difference: -0.58 [95% CI, -0.83 to -0.34]; N=471; k=4 and Hamilton Depression Scale mean difference: -2.25 [95% CI,-4.09 to -0.41]; N=262; k=3), clinical response (3 studies with statistically significant results using varying thresholds), and loss of diagnosis (RR: 1.73 [95%] CI, 1.00 to 3.00; N=395; k=4) but no statistically significant differences for other measures. The evidence suggested statistically pharmacotherapy was associated with improvement for one measure of symptoms (Children's Depression Rating Scale-Revised [CDRS-R] mean difference -3.76 [95% CI, -5.95 to -1.57, N=793; k=3), and pharmacotherapy was associated with improvement for remission, but the pooled differences were not statistically significant. The single collaborative care trial (N=101) found that collaborative care was associated with improved symptoms at 6 months (CDRS-R change: 8.5 [95% CI, 13.4 to -3.6]), response by 12 months (odds ratio [OR] for ≥50% reduction in CDRS-R score: 3.3 [95% CI, 1.4 to 8.2], and remission (OR for Patient Health Questionnaire-9 <5 at 6 months: 5.2 [95% CI, 1.6 to 17.3]). The study reported no statistically significant benefits on measures of functioning.

Twenty studies (19 randomized controlled trials and 1 meta-analysis) addressed harms. Of these, two reported on suicide risk interventions (N=885), 11 on anxiety treatment (N=1,293), and seven on depression treatment (N=1,352).

Two RCTs of interventions to reduce suicide risk or self-harm reported no statistically significant differences in adverse events.

Of the 11 RCTs reporting harms of anxiety treatments, four evaluated CBT; six evaluated pharmacotherapy; and one evaluated CBT, sertraline, and their combination. The evidence from CBT studies yielded inconsistent results on suicide-related events; these studies also suggested lower rates of withdrawal due to adverse events and serious adverse events in the CBT arms. Suicide-related events and withdrawals due to adverse events in pharmacotherapy studies were

rare and not statistically significant; however, they were more commonly reported in pharmacotherapy arms when compared with placebo arms.

Of the seven studies reporting harms of depression treatment, three evaluated pharmacotherapy; two evaluated psychotherapy; one evaluated CBT, fluoxetine, and their combination; and one evaluated collaborative care (1,276 from trials). Suicide-related outcomes, withdrawal as a result of adverse events, and serious adverse events were not statistically significant between study arms but were more frequent for pharmacotherapy when compared with placebo; inconsistencies in the evidence further reduced certainty. The evidence from the collaborative care study was inconsistent.

Limitations: No studies were available that reported benefits of screening compared with no screening. Limited evidence was available on harms of screening, long-term outcomes, test accuracy, and suicide risk and depression treatment in children. Treatment-as-usual comparators for suicide risk interventions included active treatments. The review was limited to drugs approved for pediatric use by the Food and Drug Administration (FDA). For anxiety, psychotherapy was limited to CBT.

Conclusions: We found no eligible studies that reported on benefits directly arising from screening when compared with usual care or no screening. Limited direct evidence suggests no short-term harms from screening for suicide risk. The evidence for screening for suicide risk, anxiety, and depression in children and adolescents relied on indirect evidence on the accuracy of screening and the benefits and harms of treatment. The evidence suggests that some screening instruments are reasonably accurate for anxiety and depression, but the evidence is limited for suicide risk screening instruments. Both pharmacotherapy and psychotherapy treatments have some benefit for some depression and anxiety outcomes (specifically, CBT for anxiety alone was reviewed); the evidence is limited for suicide risk interventions. Harms are rare in treatment studies but more frequent in pharmacotherapy arms when compared with placebo. Evidence gaps persist in children younger than age 11 years for test accuracy; depression and suicide risk interventions; and screening and treatment differences by sex, race/ethnicity, sexual orientation, and gender identity.

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Chapter 1. Introduction

Scope and Purpose

The United States Preventive Services Task Force (USPSTF) will use this report to issue updated recommendations for screening for suicide risk and depression in children and adolescents and to consider a new recommendation for screening for anxiety in this population. In 2014, the USPSTF concluded there was insufficient evidence to assess the balance of benefits and harms of screening for suicide risk in adolescents, adults, and older adults in primary care (I statement). In 2016, the USPSTF issued a recommendation for screening for major depressive disorder (MDD) in adolescents ages 12 to 18 years, noting that screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate followup (B recommendation). The USPSTF also concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for MDD in children ages 11 years or younger (I statement). The current review focuses on evidence for screening for suicide risk, anxiety, and depression in children and adolescents because screening instruments, implementation of screening, and outcomes for these conditions have overlap. Mental health conditions in children and adolescents may present as physical symptoms and may occur concurrently, presenting primary care physicians with opportunities to screen for one or more conditions. The review includes studies of benefits and harms of screening, accuracy of screening, and benefits and harms of treatment.

Condition Definition

Suicide

Suicide is defined as a death caused by self-inflicted injurious behavior with the intent to result in death because of the behavior.^{2,3} Suicidal attempts and ideation occur more frequently than deaths from suicide. Suicide attempts refer to nonfatal, self-directed, and potentially injurious behavior that is intended to result in death. Suicidal ideation refers to thinking about, considering, or planning suicide.⁴ Self harm may occur with or without suicidal intent. Nonsuicidal self-injury (self-harm without the intent to cause one's own death) may predict^{5,6} or co-occur⁷⁻¹⁰ with suicidal ideation and behavior. Definitions of self-harm or self-directed violence can vary widely,² and nonsuicidal self-injury may not always be distinguished from self-harm with suicidal intent. A common measure, deliberate self-harm, does not always specify intent¹¹ and can also predict suicide attempts.¹² The scope of this review includes suicide, suicide attempts, suicidal ideation, and deliberate self-harm.

Anxiety

Although anxiety as a response to stress is normal, anxiety disorders are characterized by greater duration or intensity of impairment. The *Diagnostic and Statistical Manual-5* (DSM-5)¹³ recognizes seven different types of anxiety disorders in children and adolescents: generalized

anxiety disorder (GAD), social anxiety disorder, panic disorder, agoraphobia, specific phobias, separation anxiety disorder, and selective mutism. Categories that were included under anxiety disorders in previous editions of the DSM but are no longer included as part of DSM-5 anxiety disorders are obsessive-compulsive disorder (OCD), acute stress disorder, and posttraumatic stress disorder. The scope of this review includes studies focusing on one or more anxiety disorders, defined by the DSM criteria at the time of the study, as long as the study did not focus on OCD, acute stress disorder, or posttraumatic stress disorder.

Depression

Depression is a mood disorder marked by symptoms related to how a person feels, thinks, and goes about their daily activities. According to DSM-5, MDD in children and adolescents is characterized by mild to severe persistent feelings (at least 2 weeks) of sadness or a lack of interest or pleasure in everyday pursuits, irritability, poor concentration, and somatic complaints such as difficulty sleeping, decreased energy, and changes in appetite. The scope of this review includes studies in which the majority of participants had MDD.

Etiology, Natural History, and Risk Factors

Substantial comorbidity exists between anxiety, depression, and suicide. However, differences in the pattern of overlap indicate that adolescents with depression are more likely to exhibit comorbid anxiety than the converse. ¹⁴ Moreover, evidence (from the Great Smokey Mountains Study) indicated that children who were depressed with comorbid anxiety, specifically GAD, had a higher risk of suicide than children with pure anxiety disorders. ¹⁵ Yet, across all three conditions, adverse childhood experiences influenced the likelihood of suicide, anxiety, or depression. These experiences may arise from a complex and interacting set of familial, peer, or societal factors and may vary by race and ethnicity. Additionally, individual factors, including age, sex, gender identity and sexual orientation, and genetic predisposition, also may serve as risk factors across all the conditions. These mental health conditions have long-term effects that may include chronic mental and physical health conditions, functional impairment, increased risk for substance abuse, and premature mortality. ¹⁶⁻¹⁹

Suicide

Although young children rarely attempt or die by suicide, they do reveal some preoccupation with death or suicide, either in talk or in play, and these themes are considered to signal major depression in preschool children^{20, 21} and are a significant predictor of future suicidal ideation and other psychiatric disorders.²² More commonly, suicidal behaviors first emerge during later childhood and adolescence.^{22, 23} Studies of Canadian²⁴ and U.S. adolescents²³ showed that the prevalence of attempts among ideators was 25.5 percent in the Canadian cohort and 33.9 percent in the U.S. cohort; the gender difference in prevalence was only significant in the U.S. sample. Notably the prevalence of attempts was 3 times as great in those with a plan (60.8%) as in those without a plan (20.4%). A third cohort study found that 20.6 percent of youth who both reported

suicidal ideation and reported nonsuicidal self-harm went on to attempt suicide compared with 1.4 percent of youth who did not report either ideation or nonsuicidal self-harm.²⁵

The most substantial risk factors for youth suicide are adverse childhood experiences and mental health disorders, including family history of suicide or mental health disorders, previous suicide attempts, life stressors such as interpersonal losses, legal or disciplinary problems, history of trauma, and parent-child conflict. ²⁶⁻²⁹ Suicide risk varies by gender or sex and type of behavior (note that some studies may use sex and gender terms interchangeably; the following discussion uses the language in the original publications). Males had a higher rate of suicide (17.9 per 100,000) than females (5.4 per 100,000) in 2017. ³⁰ However, the risk of suicide attempts was greater in females than males. ³¹ Lesbian, gay, bisexual, transgender, and queer (LGBTQ) adolescents exhibit elevated rates of suicide ideation and attempts compared with heterosexual adolescents. ^{11, 32, 33} One study of adolescents who identified as LGBTQ found that they were victimized more often by other youth, and peer victimization was associated with suicidal ideation and attempts, suggesting one reason for the higher suicidality rate in this population. ³⁴

Major depression as a risk for suicide may have a different role in childhood versus adolescence. In one large epidemiologic sample, ³⁵ suicide attempts in children younger than age 13 years were more strongly related to child maltreatment compared with adolescents for whom suicide attempts were more strongly related to depression. In adolescents, continuity of depression has been found to place youth at greater risk for suicidal ideation, nonsuicidal self-harm, and suicide attempts. ³⁶ Other factors associated with suicidal ideation and attempts include physical and sexual abuse; bullying; social isolation and loneliness; impulsivity; very high or very low engagement in health behaviors, low concentrations of serotonin metabolism; and variations in genes related to serotonin synthesis, transport, signaling, and catabolism. ^{11, 24, 37-44}

Anxiety

Data from the Oregon Adolescent Depression Project reported that the incidence of the first episode of anxiety was higher in childhood (ages 5 to 12.9 years) than in adolescence (ages 13 to 17.9 years), and an anxiety disorder emerging in childhood or adolescence increased the likelihood of future anxiety disorder. Several reviews of anxiety disorders in children and adolescents reported longitudinal associations of anxiety disorders over time both with the same disorder and other anxiety or depressive disorders, suggesting the heightened risk for secondary depression. The earliest emerging anxiety disorder in childhood is separation anxiety disorder. Other anxiety disorders with emergence in preschool and early school years include selective mutism and GAD, whereas social anxiety and specific phobias generally develop during the later school years. Other anxiety of the later school years.

Important risks and correlates of anxiety disorders include genetic, personality, and environmental factors. Studies have reported genetic contributions to the development of anxiety. ⁵¹⁻⁵³ Behavioral inhibition is a risk factor for developing anxiety disorders, particularly social anxiety, ^{47, 51, 54, 55} as is harm avoidance. ^{51, 56} Attachment difficulties are also associated with social anxiety. ⁵⁶⁻⁵⁸

Although many factors can contribute to the development of anxiety disorders in children, some studies and reviews have reported links between the development of anxiety disorders and parenting characteristics such as overprotection 49, 51, 52, 59, 60 and interparental conflict. 52, 60 As with other psychopathological disorders, adverse environmental conditions such as early parental separation, child maltreatment, and traumatic parental death, as well as poverty and low socioeconomic status (SES), were cited as contributing to the development of anxiety disorders. 46, 53, 59 Lastly, a higher prevalence of anxiety has been found in youth with low SES compared with youth with higher SES. 53

Depression

Although there is evidence that depression can emerge as early as 3 years of age, ⁶¹⁻⁶³ the first diagnosis of depression is more common in adolescence or adulthood than childhood. ⁶⁴⁻⁶⁶ However, studies also showed substantial continuity of depression from preschool to school age, with the likelihood of school-age depression almost 3 times as great in children with preschool-onset depression. Studies have also found that adolescents with a diagnosis of depression are more likely to have depression at a later time, ^{67, 68} up to 4 times as likely in one study as those with no psychiatric disorder. ⁶⁷

Several studies have found substantial comorbidity between depression and other psychiatric disorders. Preschool-age children with depression were also 3.5 times as likely to develop school-age anxiety disorder and 3.7 times as likely to develop school-age attention-deficit/hyperactivity disorder than children without preschool depression. Children and adolescents with depression had a greater likelihood of having a concurrent anxiety disorder, both about 4 times greater in one cohort. Other concurrent psychiatric disorders found in children and adolescents with depression include oppositional defiant disorder and substance use disorder. Gender-specific comorbidities found in one study included substance use disorder (males) and conduct disorder (females). Adolescents with past depression were more than twice as likely to have anxiety at a later time point.

Risk factors for depression include individual factors (genetics, biology, affect, cognition, behavior) that interact with social contextual factors at the proximal level (peers, family, school) and distal level (neighborhood, culture, government).^{70, 71} Individual risk factors for depression in youth include genetic predisposition, female gender, and increasing age.^{57, 72} Other risk factors include bullying, either as perpetrators or as victims, adverse life events, early exposure to stress, maltreatment, and an insecure parental relationship.⁷³⁻⁷⁵ Risk factors are also believed to interact to increase the odds of depression;^{66, 74, 76-78} additionally, maltreatment can reduce the effectiveness of evidence-based interventions.⁷⁵

Prevalence and Burden

Suicide

Suicide Deaths

Suicide is the second leading cause of death among youth ages 10 to 19 years. 79 Using the Centers for Disease Control and Prevention's (CDC's) Web-based Injury Statistics Ouery and Reporting System (WISQARS) data from 2019,80 a total of 2,744 youth ages 10 to 19 years died by suicide, of which 534 were younger youth (ages 10 to 14 years of age) and 2,2210 were older adolescents (ages 15 to 19 years). This translates to a suicide rate for children and younger adolescents, ages 10 to 14 years, of 2.6 per 100,000. The comparable rate for males and females ages 10 to 14 years was 3.1 per 100,000 and 2.0 per 100,000, respectively. Older adolescents, ages 15 to 19 years, died by suicide at a rate of 10.5 per 100,000, and the rate for males was more than 3 times that of females: 15.8 per 100,000 for males and 5.0 per 100,000 for females. In youths ages 10 to 14 years, White children and younger adolescents have a similar rate of dying by suicide compared with Black children and adolescents of the same age: 1.3 versus 1.4 per 100,000 for White and Black children, respectively; however, the suicide rate among White adolescents is nearly double the rate for Black adolescents: 8.4 per 100,000 and 4.2 per 100.000, respectively. More concerning is the upward trend in suicide rates for Black youth; from 2003 to 2017, the data show that the largest change was in the 15- to 17-year-old group (4.9%) and among females (6.6%).⁸¹ Overall, American Indian children and adolescents die by suicide at the highest rates: 2.5 per 100,000 and 16.1 per 100,000, in the younger and older age groups, respectively⁸⁰ In 2015, 16 percent of the suicides in youth ages 15 to 17 years were lesbian, gay, bisexual, transgender, and queer or questioning (LGBTQ), and 24 percent of the suicides in children ages 12 through 14 years were LGBTQ children.⁸²

Suicide Attempts

In 2019, results from the Youth Risk Behaviors Surveillance (YRBS) survey³ indicated that 8.9 percent of students (grades 9 to 12) had attempted suicide in the prior 12 months. Prevalence of suicide attempts was highest among female (11.0%), Black (11.8%), and LGBTQ students (23.4%).⁸³ The most recent data on suicide behavior in LGBTQ youth is from the 2020 National Survey on LGBTQ Youth Mental Health conducted by the Trevor Project.⁸⁴ This survey found that 20 percent of transgender and binary youth ages 13 to 24 years reported suicide attempts in 2020, and 21 percent of Black LGBTQ youth attempted suicide. In the Profiles of Study Life: Attitudes and Behaviors Survey of Adolescents 11 to 19 years conducted between 2012 and 2015, male transgender adolescents experienced the highest rate of attempted suicide of 50.8 percent, whereas male adolescents irrespective of sexual identity had the lowest prevalence rate, 9.8 percent.⁸⁵

Suicidal Ideation

Data from the 2019 YRBS^{3, 86} indicate that 18.8 percent of youth in 9th through 12th grade seriously contemplated attempting suicide, and 15.7 percent made a suicide plan. Students attempting suicide or making plans were more likely to be female, White, or LGBTQ. Data from

the 2020 National Survey on LGBTQ Youth Mental Health indicate that 42 percent of LGBTQ youth ages 13 to 24 years seriously contemplated suicide. ⁸⁴ In addition, 52 percent of transgender and binary youth seriously considered suicide, whereas the percentage of cisgendered LGBTQ youth who considered suicide is 32 percent. Forty-seven percent of Black LGBTQ youth seriously considered suicide as compared with 39 percent of White LGBTQ youth.

Importantly, two recent studies^{87, 88} found discordant reports of parent and youth reporting of suicidality. Specifically, both studies found that parents were often unaware of their child's suicidal ideation and/or attempts, and the Jones study⁸⁸ found that youth often denied having suicidal thoughts even though their parents reported suicidality. This discordance in reports between parents and children suggests that children at risk for suicide may go undetected.

Anxiety

Estimates from the 2020 National Survey of Children's Health (NSCH) were that 7.8 percent of children ages 3 to 17 years had a current anxiety disorder; 0.7 percent reported severe anxiety. Reports using the older 2016 NSCH provided comparisons by demographic factors, indicating no statistically significant differences in prevalence rates between males and females. Anxiety problems were most common among non-Hispanic White children compared with children of other racial/ethnic backgrounds and in older (ages 12 to 17 years) as compared with younger children (ages 3 to 5 years and ages 6 to 11 years). Data from the National Survey on LGBTQ Youth Mental Health indicated that 72 percent of LGBTQ youth reported symptoms of GAD, and 77 percent of transgender and nonbinary youth reported GAD symptoms.

Depression

The NSCH provides parent-reported diagnosed depression for children ages 3 through 17 years. 89 In 2020, 3.4 percent of U.S, children were estimated to currently have depression, and 0.3 percent were considered to be severe. Comparisons between groups based on demographic categories that are available from the 2016 NSCH indicated that depression was significantly more common among adolescents ages 13 to 17 years as compared with younger groups and in non-Hispanic Whites as compared with Hispanic and non-Hispanic Black youth. 90 Other U.S. depression estimates relying on adolescent self-report come from the National Survey on Drug Use and Health (NSDUH). 91 The NSDUH, an annual survey of children ages 12 to 17 years, reported the prevalence of a major depressive episode (MDE) in the past year and MDE with major impairment. An MDE is defined as follows: in the past 12 months as one or more periods of at least 2 weeks when the youth felt depressed or lost interest or pleasure in daily activities for most of the day, nearly every day as well as problems with sleeping, eating, energy, concentration, self-worth, or having recurrent thoughts of death or recurrent suicidal ideation. An MDE with severe impairment is defined a depression caused severe problems with the youth's ability to do chores at home, do well at work or school, get along with their family, or have a social life. In the 2019 NSDUH, past-year prevalence of an MDE was estimated as 15.7 percent (or 3.8 million adolescents) and MDE with severe impairment was 11.1 percent (or 2.2 million adolescents). The prevalence of depression in primary care settings may be up to twice as high as in community samples of children and adolescents. 61, 63-65

Mental Health Disorders and Racial Disparities

As noted previously, the rate of suicide deaths is highest among American Indian vouth⁸⁰ (but may vary by tribe and geographic setting)⁹² and lowest among Black youth when compared with White youth. Previous studies suggested Black youth may have had lower rates of mental health disorders when compared with White youth, but more recent cohorts of Black adolescents or children have reported having a higher prevalence of suicide rates, 80,93 increase in suicide attempts^{58, 94, 95} and anxiety disorders^{90, 96} and greater increases in the prevalence of depression than in the past. ⁹⁶ Multiple factors, including socioeconomic status, childhood adversity, family structure, and neighborhood effects, may influence patterns of prevalence by race or ethnicity. The effects of racial disparities and structural racism intersect with these factors. 97 Researchers noted the familial and societal impact of mass incarceration among Black males (rates of imprisonment among Black males increased by 3 times between 1969 and 1999), higher rates of increase in child poverty for Black children, higher rates of unemployment for Black adults, and a decline in the percentage of Black parents with college degrees. 96 An increase in nonmarital births resulting in increasing prevalence of single-parent households may also play a role in the increase in the prevalence of depression. ⁹⁶ For U.S. adults, access to financial (income), physical (home ownership), and social assets (marital status and education) may explain part of the differences in prevalence between non-Hispanic Black and Hispanic persons when compared with White persons. 98 Whether the relationship for family income holds for children and adolescents requires further research: one study suggested that higher household income may be associated with a higher risk of MDD among African American males, possibly because of the more frequent exposure to racial discrimination and reduced availability of social support from the African American community. 99, 100 In addition to these larger societal risk factors, other risk factors may include lack of access to health insurance, providers, medication (resulting in lower rates of treatment for non-White populations); 101 underdiagnosis (e.g., because of implicit clinician bias); 102 overdiagnosis (e.g., of conduct disorders instead of mood disorders); 103 and misdiagnosis (because of lack of equivalence in assessment measures). 101, 104

A culturally informed Adverse Childhood Experiences (ACEs) model posits that racial discrimination is an adverse childhood experience that influences mental and behavioral health in youth. These experiences may be blatant or subtle (e.g., microaggressions), repeated or distinct, time limited or prolonged, but they are all potentially traumatic events that, in the context of historic trauma, structural racism, and biopsychological vulnerability, can worsen mental health outcomes. When coupled with well-documented lower engagement with mental health services, these higher rates point to a high level of unmet need in Black youth.

Similar patterns of historic trauma, ACEs, and substance abuse may explain higher rates of mental health disorders in American Indian/Alaska Native youth;^{92, 111, 112} specific risk factors and their variation by tribe or geography are less well studied.

Rationale for Screening and Screening Strategies

Screening for suicide risk, anxiety, and depression is intended to identify these conditions in children and adolescents not already identified as having the condition and then engage them

effectively in confirmatory diagnostic evaluations, referrals, followup, or treatments as needed. Research has suggested that about half of adolescents with depression are not diagnosed until adulthood. 113 Screening may be particularly effective for these mental health conditions given the stigma associated with seeking care for such conditions. Although depression is common, only 2 to 3 percent of adolescents present with a primary psychiatric complaint; many present as physical problems. 114-116 A longitudinal study of deaths by suicide between 2000 and 2010 across health maintenance organizations in 11 States found that although only 16.3 percent of persons younger than age 20 years who died by suicide had a mental health visit in the 4 weeks before death, 37.9 percent used any healthcare services. In the 52 weeks before death, these rates were even higher for any use of healthcare services at 77.4 percent; 31.8 percent had a mental health visit. 117 These patterns suggest a role for screening in primary care. However, to realize the benefits of screening, effective treatment must be available that the family and child or adolescent are willing to engage in. Evidence suggests that mental health specialty care completion rates are low for youth referred from general medical settings. ¹¹⁸ This loss to followup between identification and treatment completion may pose a particular challenge for persons who are screen detected, where the net benefit of treatment may be lower than in persons who present with clinically overt symptoms.

Screening Strategies

The nature of the target conditions (suicide risk, anxiety, depression) requires patient- or caregiver-reported screening instruments. Although many instruments have been developed to assist with diagnostic evaluation for mental health conditions or broad-based socioemotional behavior and function, not all are feasible for screening in primary care settings because of length. Many instruments that are used for screening for depression and anxiety were initially developed for epidemiologic studies for surveillance or to evaluate response to treatment. Most depression instruments evaluate for common symptoms related to depression and also include one or more items related to suicidal ideation. Anxiety instruments are more heterogenous, some are designed to evaluate for a specific anxiety disorder (e.g., social anxiety disorder), while others are designed to evaluate across the breadth of existing anxiety disorders. Assessments designed to evaluate youth suicide risk typically involve one component related to evaluating current ideation and self-harm behaviors, but also involve an assessment for past attempts and behaviors given the strong correlation between past behaviors and future risk. Instruments designed to screen across conditions may be more efficient than instruments targeting single conditions; however, trans-condition instruments are longer and require more time to administer, reducing feasibility in primary care settings and may be less accurate for any specific condition.

Treatment Approaches

Suicide

Therapeutic interventions targeting at-risk youth include psychotherapy and pharmacotherapy. ¹¹⁹, These therapies seek to reduce suicidal ideation, behaviors, and attempts. Psychotherapeutic approaches may include short-term psychoeducation or longer-term interpersonal psychotherapy, cognitive behavioral therapy (CBT), dialectical behavioral therapy (DBT), mentalization therapy,

and trauma-informed therapy. Pharmacotherapy may include antidepressants, antipsychotics, and mood stabilizers. In addition to these treatments, safety planning interventions, which generally include caregivers, may also be designed to reduce the access to or lethality of means of suicide. These therapies may be combined with interventions to address social determinants of health. For example, individually focused interventions that primary care providers can participate in or provide referrals to may seek to educate families of those in crisis about safely storing medications and firearms, distributing gun safety locks, and removing other items that could be used for an attempt. 121, 122

Anxiety

Treatments for anxiety disorders includes psychotherapy, pharmacotherapy, and combinations. ¹²³ CBT is among the most commonly used approach, but other approaches include parent-child interaction therapy, problem-solving therapy, DBT, exposure therapies, hypnosis, social skills training, mindfulness therapy, psychodynamic psychotherapy, family therapy, attention modification program, motivational interviewing, trauma-informed therapy, and eye movement desensitization reprocessing therapy. ¹²⁴⁻¹²⁷ Duloxetine, a serotonin–norepinephrine reuptake inhibitor (SNRI), is the only Food and Drug Administration (FDA)-approved medication for GAD in children age 7 or older. Pharmacological interventions prescribed on an off-label basis include selective serotonin reuptake inhibitors (SSRIs); other SNRIs; benzodiazepines; tricyclic antidepressants; and other drugs such as mebicarum, buspirone, mirtazapine, and nefazodone.

Depression

Treatments for MDD includes psychotherapy, pharmacotherapy, and combinations. 128-130 Different types of psychotherapy are used in treating children and adolescents with depression, but CBT and interpersonal therapy (IPT) have the most evidence supporting their effectiveness. 131-133 Other types of therapy used clinically for treating depression include supportive psychotherapy, family therapy, psychodynamic therapy, behavioral therapy, DBT, and trauma-informed therapy. 134 Although several antidepressants are approved for treating MDD in adult populations, fluoxetine is the only medication that the FDA has approved for use in treating MDD in children age 8 years or older. In addition, the FDA has approved escitalopram to treat MDD in adolescents ages 12 to 17 years. Other medications may sometimes be prescribed to children on an off-label basis including sertraline (approved in persons 6 years or older for obsessive-compulsive disorder [OCD]), fluvoxamine (approved in persons 8 years or older for OCD), and clomipramine (approved in persons 10 years or older for OCD). 135 In 2003, the FDA recommended that paroxetine not be used for treating MDD in children and adolescents because of reports of possible suicidal ideation and suicide attempts in children and adolescents taking paroxetine for depression. In 2004, the FDA issued a public warning about an increased risk of suicidality in children and adolescents treated with all antidepressants. The FDA currently requires these medications to carry a boxed warning about the potential danger of suicidality.

Clinical Practice in the United States

Evidence is limited on the implementation of routine screening in the United States. One survey of 727 primary care physicians in the United States in 2003 and 2004 found that 76 percent believe in the importance of talking to adolescent patients about their mental health, but only 46 percent said that they always asked their patients about their mental health. Analysis of data from the 2005 to 2010 National Ambulatory Medical Care and National Hospital Ambulatory Medical Care Survey found that depression screening occurred in as few as 0.2 percent of visits, with variations by race/ethnicity and region. The study reported lower odds of screening among Hispanic patients than White non-Hispanic patients and lower odds in the West compared with the Northeast. More recent insurance claims data (2010 to 2014) for 12- to 14-year-old adolescents with private insurance also indicated low rates of coding for depression screening at 1.8 percent. Evidence on the rates of screening for other disorders were also limited and, when available, indicated low rates of screening ranging from 10 percent or less among pediatric emergency medicine physicians to 23 percent in the primary care setting.

Recommendations of Other Organizations

Suicide

Guidelines for screening for suicide are described in **Table 1**. The American Academy of Family Physicians follows the USPSTF recommendation. The American Academy of Pediatrics (AAP) recommends universal screening for suicide youth 12 years of age and older and screening when clinically indicated for youth 8 to 12 years of age. For younger children (younger than age 8), the guidelines recommend assessing for suicidal thought and behaviors if warning signs exist. The American Academy of Child and Adolescent Psychiatry (AACAP) policy statement supports screening for suicide risk across physical and mental health settings. The Joint Commission recommends that organizations screen all individuals for suicidal ideation using a validated screening tool. 144

Anxiety

AACAP notes the lack of empirically based guidelines on screening but offers resources for screening.¹⁴⁵ The National Institute for Health and Clinical Excellence (NICE) recommends screening.¹⁴⁶

Depression

U.S.-based guideline groups (Guidelines for Adolescent Depression in Primary Care [GLAD-PC, supported by AAP, AACAP, and the American Psychiatric Association]¹⁴⁷) recommend routine screening for depression. The Canadian Task Force is updating its guidelines, ¹⁴⁸ which earlier rated the evidence as insufficient. ¹⁴⁹

Multiple Psychiatric Conditions

AAP-Bright Futures¹⁵⁰ and the American College of Obstetricians and Gynecologists¹⁵¹ are consistent in recommending screening for emotional and behavioral issues, with followup diagnostic and treatment services (**Table 1**).

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Chapter 2. Methods

Key Questions and Analytic Framework

The scope and key questions (KQs) were developed by the Evidence-based Practice Center (EPC) investigators, USPSTF members, and Agency for Healthcare Research and Quality (AHRQ) Medical Officers. **Figure 1** depicts the analytic framework and KQs that guided the review.

Five KQs were developed for this review:

- 1. Do depression, anxiety, or suicide risk screening programs in primary care or comparable settings result in improved health outcomes in children and adolescents?
- 2. Do instruments to screen for depression, anxiety, or suicide risk accurately identify children and adolescents with depression, anxiety, and increased risk of suicide in primary care or comparable settings?
- 3. What are the harms associated with screening for depression, anxiety, or suicide risk in primary care or comparable settings in children and adolescents?
- 4. Does treatment (psychotherapy, pharmacotherapy, or collaborative care) of depression, anxiety, or suicide risk result in improved health outcomes in children and adolescents?
- 5. What are the harms of treatment (psychotherapy, pharmacotherapy, or collaborative care) in children and adolescents who are treated for depression, anxiety, or suicide risk?

In addition to addressing the KQs, this review also looked for evidence related to six contextual questions (CQs):

- 1. What is the diagnostic yield from screening for depression, anxiety, or suicide risk in typical primary care practice settings?
- 2. What are the minimal clinically important differences (the smallest value of benefit to patients) for symptoms and functioning on the most common instruments used to measure response to treatment of depression, anxiety, or suicide risk?
- 3. What are the U.S. FDA boxed warnings for pharmacotherapy for the treatment of depression, anxiety, or suicide risk in children and adolescents?
- 4. What psychotherapies other than CBT are used to treat anxiety in children and adolescents?
- 5. What is the effectiveness of evidence-based treatment in children and adolescents with persistent depressive disorder (PDD) and depressive disorders not otherwise specified (DDNOS)?
- 6. What proportion of children and adolescents who screen positive for depression, anxiety, or increased suicide risk engage with care (i.e., return for clinical evaluation and treatment)?

These CQs were not a part of this systematic review. They are intended to provide additional background information. **Appendix A** presents a summary of the literature addressing these questions.

Data Sources and Searches

This review includes three conditions and builds on prior reviews for the USPSTF for suicide risk¹¹⁹ and depression, ¹⁵² and AHRQ Effective Healthcare Program (EHC) reviews on anxiety ¹²³ and depression. 153 As a result date limits vary by topic and database. PubMed and the Cochrane Library were searched on April 28, 2020. PsycINFO and CINAHL were searched on April 30, 2020. Depression searches were limited to articles published from January 1, 2015 to April 28, 2020; anxiety searches were limited to articles published from January 1, 2017 to April 28, 2020; and suicide risk searches were limited to articles published between June 1, 2012 to April 28, 2020. We conducted a bridge search on July 19, 2021, and surveillance through June 1, 2022. Search terms and Medical Subject Headings (MeSH) focused on terms that describe relevant populations, tests, interventions, outcomes, and study designs was used when applicable. The search relied primarily on the previous systematic reviews for the USPSTF (depression, ¹⁵² suicide¹¹⁹) and the AHRQ EHC (anxiety¹²³) to identify potentially relevant studies published before the last search data in each of the three reviews. Complete search terms and limits are listed in **Appendix B**. ClinicalTrials.gov was searched for unpublished literature. To supplement electronic searches, reference lists of relevant articles, systematic reviews, and studies meeting the inclusion criteria were reviewed.

Study Selection

We developed inclusion and exclusion criteria for populations, interventions, comparators, outcomes, timing, settings, and study designs with input from the USPSTF (**Appendix C**). We included English-language studies of children and adolescents age 18 years or younger on average conducted in countries categorized as "very high" on the 2019 Human Development Index.¹⁵⁴

When possible, we aligned inclusion and exclusion criteria across the three conditions (suicide risk, anxiety, depression), with the exception of three criteria. First, population inclusion criteria were broader for depression treatment studies (KQs 4 and 5) than for anxiety or suicide risk. For depression, although the population criterion focuses on MDD (as defined by the DSM), we included treatment studies that had as few as 51 percent of participants with MDD to include studies with participants with PDD or DDNOS. This approach ensures consistency with the prior USPSTF review on screening for depression in children. Furthermore, we addressed the effectiveness of treatment for PDD and DDNOS in a CQ. For other conditions, we required that treatment studies limit participants to those with anxiety disorder or with increased suicide risk. As noted earlier, anxiety disorders can vary widely, and their onset may vary by age. Given this heterogeneity, eligible anxiety disorders included GAD, social anxiety disorder, panic disorder, agoraphobia, separation anxiety disorder, and selective mutism. Definitions for increased risk of suicide varied by study but could include suicidal ideation (suicidal thoughts or plan for suicide), history of suicide attempts (nonfatal, self-directed, and potentially injurious behavior that is intended to result in death), and deliberate self-harm.

Second, for depression and suicide risk interventions, we were more inclusive of a wide range of psychotherapy, counseling, and care delivery models (such as collaborative care and care

management) than for anxiety. For anxiety, we limited nonpharmacological interventions to CBT in the interest of efficiency.

Third, we were more inclusive of a wide range of comparators for suicide risk interventions. We included treatment-as-usual comparators because ethical concerns limit the ability to conduct comparative studies using placebo or wait-list controls. For depression and anxiety interventions, we restricted comparators to placebo, wait-list, no intervention, attention control, and usual care. We did not include treatment-as-usual studies in specialist settings for these conditions because the comparison may understate the benefits of screening in primary care where the comparison is likely to be usual care in primary care settings.

Fourth, we accounted for the condition in assessing the accuracy of screening. For anxiety and depression, we required eligible studies to compare the accuracy of screeners with structured clinical interviews using standard diagnostic criteria. For suicide risk, however, we required the screener to be compared with an assessment of increased suicide risk based on an interview by a qualified professional.

For all conditions, a priori priority subpopulations of interest included younger age (children vs. adolescents), race/ethnicity, sex, gender identity, and sexuality. We limited pharmacotherapy to pharmacotherapy agents approved for pediatric use (e.g., clonidine, duloxetine, fluoxetine, escitalopram, sertraline, fluvoxamine). Interventions were required to be relevant to or referable from primary care; school-wide and community screening and interventions were excluded as a result. Eligible health outcomes across all conditions for KQ 1 and KQ 4 (screening and treatment benefits) included depression or anxiety symptoms as measured through validated instruments, clinical response, or remission; suicide deaths, suicide attempts and deliberate selfharm or suicidal ideation; all-cause mortality; quality of life measured using validated scales or instruments; and functioning (using validated scales or instruments, days of missed school, sleeprelated outcomes). Eligible harms included treatment avoidance, deterioration in patient-provider relationship, labeling or stigma, inappropriate/unnecessary treatment, serious adverse effects, withdrawals due to adverse effects, and suicidality. Eligible settings across all KQs included primary care clinics, including school-based health clinics, and virtual or community-based settings. For screening questions (KQs 1 through 3), we also included studies recruiting from general emergency departments and schools. For treatment questions (KQs 4 and 5), we also included specialty clinics. We excluded studies of school-wide screening for KO 1. We included RCTs for KQs 1, 3, 4, and 5 and diagnostic accuracy studies for KQ 2. Additionally, we included nonrandomized, controlled trials for KQ 1 and KQ 3. We included observational studies for the harms questions (KQ 3 and KQ 5). For KQ 5, we included systematic reviews of comparative cohort and case-control observational studies to capture rare harms but restricted pharmacotherapy harms studies to large (>1,000 participants) comparative cohort and casecontrol observational studies published after eligible systematic reviews.

Titles and abstracts were independently reviewed by two investigators; those marked for potential inclusion by either reviewer were retrieved for evaluation of the full text. The full texts were then independently reviewed by two investigators to determine final inclusion or exclusion. Disagreements were resolved by discussion and consensus.

Quality Assessment and Data Abstraction

For newly identified studies, two senior reviewers independently assessed each study's methodological quality using predefined criteria developed by the USPSTF (**Appendix D**) conducted using instruments devised for each of the included study designs, specifically Cochrane ROB 2.0 for randomized studies of interventions¹⁵⁵ (KQs 1, 3, 4, and 5), the ROBINS-I tool¹⁵⁶ for nonrandomized studies of interventions¹²³ (KQ 5), ROBIS for systematic reviews (KQ 5),¹⁵⁷ and the QUADAS-2 instrument¹⁵⁸ for diagnostic accuracy (KQ 2). We re-rated all previously included accuracy studies (KQ 2). We spot-checked and carried forward quality ratings of studies included in two recent AHRQ EHC reports on depression¹⁵³ and anxiety¹²³ in children and adolescents.¹⁵³ Studies reporting benefits and harms may have been assigned different quality ratings for benefits and harms. Disagreements were resolved by discussion. Only studies rated as having good or fair quality were included in the synthesis. For each included study, one investigator extracted pertinent information about the methods, populations, interventions, comparators, outcomes, timing, settings, and study designs. All data extractions were checked by a second investigator for completeness and accuracy.

Data Synthesis and Analysis

Findings for each KQ were summarized qualitatively and in tabular format. The overall strength of the evidence for each KQ was assessed as high, moderate, low, or insufficient based on the overall quality of the studies, consistency of results between studies, precision of findings, risk of reporting bias, and limitations of the body of evidence, using methods developed for the USPSTF and the EPC program. Additionally, the applicability of the findings to U.S. primary care populations and settings was assessed. Discrepancies were resolved through consensus discussion.

Additionally, when at least three independent and similar studies were available, pooled effects for relative risks for categorical outcomes and standardized and weighted mean differences for continuous outcomes random-effects models were generated using the inverse-variance weighted method of DerSimonian and Laird. Absolute risk differences were presented for outcomes with signals of benefit or harm. The clinical and methodological heterogeneity of the studies was assessed according to established guidance, ¹⁶⁰ and similarities and differences in populations, tests, treatments, comparators, outcomes, and study designs were assessed qualitatively. Statistical heterogeneity of findings was assessed with the *I*² statistic; 0 percent to 40 percent might not be important; 30 percent to 60 percent may represent moderate heterogeneity; 50 percent to 90 percent may represent substantial heterogeneity; and 75 percent to 100 percent represents considerable heterogeneity. ¹⁶¹ All quantitative analyses were conducted using Comprehensive Meta-Analysis (Version 3.3) software. ¹⁶² We considered pooled findings statistically significant when the 95% confidence intervals (CIs) excluded the null value. We assessed the potential for publication bias through visual inspection of a funnel plot when at least 10 studies were included in an analysis.

U.S. Preventive Services Task Force Involvement

The authors worked with USPSTF liaisons throughout the review process to develop and refine the analytic framework, key questions, and scope of the work. AHRQ staff provided project oversight, reviewed the report, and assisted in conducting an external review of the draft evidence synthesis.

Expert Review and Public Comment

The draft Research Plan was posted on the USPSTF website for public comment from April 30, 2020, to May 27, 2020. Regarding suggested edits to the KQs, one commenter noted that screening is intended to identify those at increased risk for any of the eligible conditions (anxiety, depression, suicide risk, or a combination), not just those at increased risk of suicide. In response, the USPSTF edited the key questions to remove the qualifier "increased risk of suicide" and instead refers to "suicide risk." One comment suggested a focus on implementation barriers rather than the effectiveness of screening. Although we agree that these factors are important, the review is intended to support a screening recommendation. Commenters suggested edits to the CQs to improve clarity. In response, we revised CQ 2 to clarify that the term "minimal clinically important differences" refers to the smallest value of benefit to patients. We revised CQ 3 and CQ 4 to specify that the population of interest is children and adolescents. We qualified CQ 5 as being limited to evidence-based treatments and clarified that engagement with care in CQ 6 refers to returning for clinical evaluation and treatment.

Regarding suggested edits to the inclusion and exclusion criteria, one commenter suggested focusing on screen-detected populations in reviewing the treatment literature. Although we agree that for treatment questions, screen-detected populations are ideal, the evidence is likely to be extremely sparse. As a result, we are not restricting treatment studies to screen-detected populations alone. One commenter suggested excluding clomipramine because it is not a first-line therapy; in response, we excluded clomipramine. Some reviewers asked about the exclusion of active comparators for treatment questions. The USPSTF considers comparative effectiveness to be outside of its scope. Commenters suggested several outcomes; in response, we have clarified that we will include validated outcomes for prespecified outcomes for KQ 1 and KQ 4 and have added false alarm and false reassurance to outcomes for KQ 3. Some comments focused on priority populations; the review will report on priority populations defined by age, sex, race/ethnicity, gender identity, and sexuality. Some comments highlighted the importance of context, applicability, type of intervention, and type of disorder. We considered these factors in the analysis, when data were available. A final research plan was posted on the USPSTF's website on August 13, 2020.

The draft evidence review was reviewed by content experts, representatives of Federal partners, USPSTF members, and AHRQ Medical Officers and was revised based on comments received. Specifically, we added followup data from an included study and revised the abstraction of an existing study. We also revised data on prevalence and burden in the introduction section. The draft evidence review will also be posted for public comment. Revisions will be made based on

comments received, a for inclusion/exclusion	and any references su on.	iggested by expert	t or public reviewer	rs will be evaluated

Chapter 3. Results

We screened 37,706 titles and abstracts and 798 full-text articles to identify 80 unique studies from 106 publications for inclusion (**Figure 2**). Since of these studies were new to the update of suicide 164, 179-181, 192, 194, 202, 212-215, 221, 222, 229, 236 and 8 primary studies and one meta-analysis were new to the update of depression. 172, 173, 176, 187, 204, 205, 216, 217, 248, 249, 266 We identified no studies reporting on the benefits (KQ 1) of screening.

We identified 17 studies on accuracy of screening (KQ 2). ^{166, 170-172, 188, 189, 199, 218, 219, 223, 230-232, 234, 235, 247, 250} Of these, one reported on suicide, ²⁴⁷ 10 on anxiety, ^{166, 171, 188, 199, 218, 219, 230-232, 250} seven on depression, ^{170, 172, 189, 199, 219, 223, 235} and two on combined screeners for anxiety or depression. ^{219, 234} Three of these studies reported on more than one condition. ^{199, 219, 234} We included two studies, both on harms of screening for suicide risk (KQ 3). ^{267, 268} Sixty studies were included for benefits (KQ 4); of these, 16 reported on suicide, ^{164, 179-182, 191-194, 197, 200-202, 212-215, 221, 222, 229, 236, 245, 265} 29 on anxiety, ^{163, 165, 167-169, 177, 178, 183, 190, 195, 196, 198, 203, 206, 220, 224-228, 237-244, ^{246, 251, 253-262} 13 on depression, ^{174-176, 185-187, 204, 205, 207-211, 216, 217, 233, 248, 249, 252, 266} and two on depression or anxiety. ^{184, 263, 264} Twenty studies were included on harms (KQ 5), including two on suicide, ^{179-181, 192} 11 on anxiety, ^{168, 169, 224-228, 238, 239, 242-244, 253-262} and seven on depression. ^{173, 176, 185, 186, 207-211, 233, 252, 266} Details of quality assessments of included studies and studies excluded based on poor quality are provided in **Appendix D**. **Appendix E** presents detailed results organized by outcome and **Appendix G** presents forest plots for meta-analyses described in Chapter 3. **Appendix H** presents results for off-target symptoms (e.g., improvement in anxiety for interventions designed to address depression). **Appendix I** presents complete evidence tables for all studies. **Appendix J** lists studies excluded at full-text screening.}

The results below present findings by KQ first, then by condition for suicide risk, anxiety, depression, and finally studies requiring dual diagnoses or including more than one diagnosis. Within each section, we describe study characteristics and results for each outcome for the overall population and for specific populations (for priority populations defined by age, sex, race/ethnicity, gender identity, and sexuality and within age groups).

KQ 1. Do Depression, Anxiety, or Suicide Risk Screening Programs in Primary Care or Comparable Settings Result in Improved Health Outcomes in Children and Adolescents?

We found no eligible studies addressing KQ 1 on direct evidence for health outcomes of screening for depression, anxiety, or suicide risk on health outcomes in primary care or primary care—relevant settings. KQs 2 and 4 provide indirect evidence by summarizing the accuracy of screening and benefits of treatment, respectively.

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KQ 2. Do Instruments to Screen for Depression, Anxiety, or Suicide Risk Accurately Identify Children and Adolescents With Depression, Anxiety, and Increased Risk of Suicide in Primary Care or Comparable Settings?

Suicide Risk

We included one fair-quality study, which was included in the previous review.²⁴⁷

Study Characteristics

The one identified study recruited participants (N=580) from seven high schools in the Pacific Northwest region of the United States. ²⁴⁷ Eligible participants were potential high school dropouts ages 14 to 20 years. Forty-two percent were female; 57 percent were White, 20 percent were African American, 14 percent were Asian American, 8 percent were Latino, and 2 percent were American Indian. Authors used the Suicide Risk Screen (SRS), a 20-item screener, that was embedded into a longer questionnaire. The screen is considered positive if the youth scores in any one of three categories designating increased risk. This study evaluated the SRS against two reference standards both of which were completed within 7 to 10 days of screening. The first reference standard was a direct suicide risk as determined during the Measure of Adolescent Potential for Suicide (MAPS) clinical interview, and the second reference standard was a clinical risk assessment (CRA) global rating made after completing the MAPS.

Results of Included Studies

The prevalence of increased suicide risk was 19 percent based on the Direct Suicide Risk reference standard and 22 percent based on the Clinical Risk Assessment reference standard.²⁴⁷ The sensitivity and specificity of the SRS against the DSR reference standard was 0.91 and 0.60, respectively.²⁴⁷ Against the CRA reference standard, the sensitivity and specificity were 0.87 and 0.60, respectively.²⁴⁷

Results: Findings for Specific Populations

Subgroup Analyses

Authors reported no results by populations of interest prespecified for this update.

Findings Within Age Groups

All studies reported results for adolescent participants.

Anxiety

Study Characteristics

We included 10 studies that assessed accuracy of screeners for detecting anxiety, ^{166, 171, 188, 199, 218, 219, 230-232, 250} all of which were of fair quality. Detailed study characteristics are provided in **Appendix I Table 1**. All 10 studies were new in this update. Three studies ^{166, 199, 230} were located in the United States; two ^{171, 188} in Spain; two ^{231, 232} in Finland; and one each in the Netherlands, ²¹⁸ United Kingdom, ²¹⁹ and Taiwan. ²⁵⁰ Six studies recruited their samples from schools; ^{171, 188, 218, 231, 232, 250} three recruited from primary care, ^{166, 199, 230} and one from hospital outpatient departments and pediatric mental health clinics. ²¹⁹

Studies examining accuracy of anxiety screeners included adolescents only ^{188, 199, 230-232, 250} and both children and adolescents. ^{166, 171, 218, 219} In studies where sex was reported, ^{166, 171, 188, 199, 218, 219, 230} the percentage of females ranged from 43 to 63 percent. In the four studies that reported race/ethnicity, ^{166, 199, 219, 230} the percentage of non-White youth ranged from 1 to 58 percent.

Index Screeners

Overall, the studies assessed 12 different screeners for detecting anxiety in youth, some of which were examined in multiple studies. Appendix E Table 1 provides a brief description of each. Three studies evaluated the Screen for Child Anxiety Related Disorders (SCARED), 166, 171, 218 administering both the parent and child versions. Canals et al 171 also assessed the SCARED short version with both parents and children respondents. Two studies evaluated the Social Anxiety Scale (SAS), one of which 166 assessed the use for children (SAS-C) and both of which assessed the version for adolescents (SAS-A). 166, 188 Whereas Bailey et al 166 administered the SAS-C and the SAS-A with both parents and children/adolescents as informants, Garcia-Lopez et al¹⁸⁸ administered the SAS-A to adolescents only. Two studies 188, 250 evaluated the Social Phobia Inventory (SPIN), and two studies 188, 232 evaluated the related Mini-SPIN, all with adolescents; however, Garcia-Lopez et al¹⁸⁸ did not report sensitivity or specificity and thus is not discussed further. One study assessed the Social Worries Questionnaire (SWQ-P), ¹⁶⁶ administering it to parents of both children and adolescents. One study each evaluated the Paediatric Index of Emotional Distress (PI-ED), ²¹⁹ the Autonomic Nervous System Questionnaire (ANS), ²³⁰ and the Patient Health Questionnaire—Adolescents (PHQ-A), ¹⁹⁹ for detecting panic disorder and GAD. One study¹⁸⁸ assessed the Social Phobia and Anxiety Inventory-Brief (SPAI-B), the Social Phobia Inventory (SoPhI), the Escala para la Detección de Ansiedad Social (EDAS), and the Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA) with adolescents. The Garcia-Lopez study¹⁸⁸ only reported area under the curve (AUC) rather than sensitivity or specificity data for the SPIN, Mini-SPIN, EDAS, LSAS-CA, or SoPhI; these data appear in the evidence tables in Appendix I Table 1 but are not discussed hereafter. The results focus on the nine instruments (comprising 15 variations) with results on sensitivity and specificity.

Reference Standards

In all cases, the diagnostic assessment used as the reference standard was a clinical interview. **Appendix E Table 2** provides a description of each interview. Three studies 166, 188, 230 used the

Anxiety Disorders Interview Schedule for DSM-IV-for Children (ADIS). One study¹⁶⁶ interviewed parents, one study²³⁰ interviewed adolescents, and one study¹⁸⁸ interviewed both parents and adolescents. Two studies^{171, 250} interviewed the children and adolescents using the MINI International Neuropsychiatric Interview for Kids (MINI-Kid). Two studies^{231, 232} used the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL). One study each interviewed the youth with the Child edition of the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* Version IV (DSM-IV) (child edition of the structured clinical interview for DSM-IV [KSCID]),²⁶⁹ the Computerized Diagnostic Schedule for Children (C-DISC),²¹⁹ and a diagnostic interview using items from several different interview schedules.¹⁹⁹ Five of the eight studies^{171, 219, 230, 250} provided information on the timing of the diagnostic assessment in relation to the screening. One study²¹⁹ clinically interviewed participants at the same time as the screener was administered, one study¹⁷¹ interviewed participants within a week of the screener administration, and four studies^{230-232, 250} administered the diagnostic assessment within a month of the screener.

Results of Included Studies

Results pertaining to accuracy are found in **Table 2** and are organized by condition. All but one study²³⁰ reported prevalence. The prevalence of anxiety disorders based on the clinical interviews ranged from 2.5 percent to 41 percent. The three studies with the highest prevalence (i.e., 20%, 24%, and 41%)^{171, 188, 218} oversampled youth with scores on the screener that were in the at-risk range; thus, we did not use these values when calculating the percentage of false-positives and false-negatives per 1,000 screens. The estimates of prevalence varied by condition. The lowest prevalence of 2.5 percent was for a study detecting GAD,¹⁹⁹ and two studies with unselected samples each had a prevalence of 13 percent, one to detect GAD^{218, 219} and one to detect social anxiety disorder.¹⁶⁶

Global Anxiety

One study evaluated the SCARED¹⁷¹ to detect global anxiety. In the study of the SCARED, the authors administered the full version of 41 items and a short 10-item version to both children and their parents. Cutoff scores to determine a positive screener varied by screener and respondent. Using the reported index test thresholds, ¹⁷¹ sensitivity ranged between 0.34 and 0.76, and specificity ranged between 0.68 and 0.87 for varying cutoffs on the screeners. With the exception of the full screener administered to children, all sensitivity values were lower than specificity values.

GAD

Three studies assessed screeners to detect GAD. One study¹⁹⁹ assessed the PHQ-A. The sensitivity was 0.5 and the specificity was 0.98. The second study²¹⁸ examined the SCARED-GAD scale, finding a somewhat higher sensitivity (0.64) but lower specificity (0.63) than the PHQ-A. The third study assessed the PI-ED (Anxiety Scale)¹⁷¹ and had a higher sensitivity (0.88) with a comparable specificity (0.85).

Panic Disorder

Two studies assessed screeners for detecting panic disorder—the ANS²³⁰ and the PHQ-A.¹⁹⁹ The study of the ANS assessed accuracy for three versions, with two, three, and four questions. The sensitivity was 1.0 for all versions, whereas the specificity ranged between 0.47 and 0.66. The PHQ-A reported a sensitivity of 0.42 and a specificity of 0.99.

Separation Anxiety Disorder

Only one study²¹⁸ examined a screener to detect separation anxiety disorder in adolescents. Using the SCARED—Separation Anxiety Scale, the study found sensitivity to be 0.88 and specificity 0.73.

Social Anxiety Disorder

Several studies reported on screeners to detect social anxiety disorder. Two studies assessed the SAS, ^{166, 188} one of which administered both the child and adolescent versions. ¹⁶⁶ The sensitivity of the SAS varied as a function of the respondent. In one study ¹⁸⁸ in which adolescents were the respondents, sensitivity was 0.93 but was 0.75 in another study ¹⁶⁶ when parents were responding about their adolescents' symptoms. Specificity in the two studies was comparable—0.80 ¹⁶⁶ and 0.78. ¹⁸⁸ Sensitivity and specificity for parent-reported social anxiety disorder in children ¹⁶⁶ was 0.78 and 0.74, respectively.

Three studies assessed the SPIN^{231, 250} or the Mini-SPIN.²³² Sensitivity was similar in the two SPIN studies: 0.82²³¹ and 0.80,²⁵⁰ as was specificity: 0.85²³¹ and 0.77,²⁵⁰ with similar thresholds for a positive screening: 24²³¹ and 25.²⁵⁰ The study examining the Mini-SPIN²³² found equally high sensitivity and specificity despite significantly fewer items (3 as opposed to 17 in the SPIN).

Reports on three other screeners to detect social anxiety disorder were in two studies. One study¹⁸⁸ found that the Social Anxiety Scale for Adolescents (SASA) had sensitivity of 0.93 and specificity of 0.79 and that the SPAI-B had sensitivity and specificity of 0.86 and 0.88, respectively. The second study¹⁶⁶ reported that the SWQ had sensitivity of 0.67 for detecting social anxiety disorder in children and 0.83 for detecting social anxiety disorder in adolescents; specificity was 0.94 in children and 0.84 in adolescents.

Any Anxiety Disorder

Two studies ^{199, 218} examined the utility of screeners to detect any anxiety disorder. One assessed the PHQ-A¹⁹⁹ for detecting either panic disorder or GAD, finding a prevalence of 5 percent, sensitivity of 50 percent, and a specificity of 98 percent. The second study²¹⁸ used the SCARED, combining the adolescents who screened positive for GAD, separation anxiety disorder, and/or social anxiety disorder. In this study, the prevalence was 20 percent, with a sensitivity of 0.88 and a specificity of 0.56.

Based on the reported sensitivity and specificity data, the number of false-negatives and false-positives per 1,000 screening tests at the lowest $(2.5\%)^{199}$ and highest $(13)^{166,\,219,\,230}$ prevalence in an unselected population reported in the included studies is presented in **Table 2**. Three studies reported a higher prevalence for anxiety, but we did not use these values because they sampled all the screen-positive cases, resulting in an artificially high prevalence value. With the exception of the scales from the PHQ-A, ¹⁹⁹ the number of false-negatives is lower than the number of false-positives.

Results: Findings for Specific Populations

Subgroup Analyses

No subgroup analyses for specific populations were reported.

Findings Within Age Groups

Seven studies reported on adolescents , and reported on eight instruments (PHQ-A, ANS, SAS, SASA, SPAI-B, SCARED-SP, SPIN, Mini SPIN) for GAD, global anxiety, panic disorder, and social anxiety disorder. ^{166, 188, 199, 230-232, 250} Inclusion criteria ranged from 12 to 18, with a mean age of 14.8.

Four studies reported on older children and adolescents on seven instruments (full scale, subscale, or short versions of SCARED, PI-ED, and SAS) for GAD, SAD, separation anxiety, and global anxiety. ^{166, 171, 270, 271} Inclusion criteria for these studies ranged 7 to 17 years, with a mean of 11.0 years.

No studies reported on younger children.

Only one study (Bailey et al. 2006¹⁶⁶) reported results separately for adolescents and children for the same instruments (SCARED-SP, SAS-A, SAS-C, and SWQ); these results did not suggest consistent differences in sensitivity and specificity by age of the children, and variations in instruments and thresholds may explain differences in results. No other studies reported on both children and adolescents for a single instrument and condition.

Across instruments and conditions, differences between studies reporting on adolescents versus adolescents and children also did not suggest age-related patterns; the wide range of instruments, thresholds, and conditions preclude making conclusions about accuracy for children versus adolescents.

Depression

We included seven fair-quality studies of diagnostic test accuracy. 170, 172, 189, 199, 219, 223, 235 Two studies were new to this update. 172, 219 Brief study characteristics are provided in **Table 3**.

Study Characteristics

Three studies were conducted in the United States, ^{189, 199, 235} and the rest were conducted in various countries in Europe ^{170, 172, 219} and Australia. ²²³ One study ²¹⁹ enrolled both children and adolescents, while the rest enrolled only adolescents. Studies enrolled boys and girls in relatively equal proportions. In the studies conducted in the United States, the proportion of participants who were Black was between 1 percent and 25 percent; in the rest of the studies, participants were nearly entirely White or race and ethnicity was not reported. Two studies recruited participants from clinical settings (primary care, ¹⁷² mix of primary care and outpatient mental health service ²¹⁹), one study recruited participants from primary care and school nurse offices, ¹⁹⁹ and the rest of the studies recruited from either school-based samples ^{189, 223, 235} or the community. ¹⁷⁰

Index Screeners

Authors of the included studies assessed seven different screening instruments (Beck Depression Inventory [BDI], ^{170, 235} Center for Epidemiologic Studies-Depression [CES-D], ^{189, 235} Clinical Interview Schedule—Revised [CIS-R], ²²³ Hopkins Symptom Checklist [HSCL], ¹⁷² PHQ-A, ¹⁹⁹ PI-ED Depression Subscale, ²¹⁹ and the World Health Organization Five Item Well-Being Index [WHO-5] ¹⁷²). Some authors assessed more than one instrument or more than one threshold for a positive screen for the same instrument. Few studies prespecified thresholds for a positive screen. **Appendix E Table 1** includes detailed screening test characteristics.

Reference Standards

Authors used clinical diagnostic interviews administered either concurrently or within 4 weeks of screening as a reference standard; most (but not all) reference standards were structured diagnostic clinical interviews tied to existing diagnostic criteria such as the DSM. Detailed reference standard information is included in **Appendix E Table 2**. All studies reported sensitivity and specificity for current MDD; many also reported positive and negative predictive value. Only one study reported results separately for boys and girls. ¹⁸⁹ No other data for specific populations were reported.

Results of Included Studies

The prevalence of major depression based on reference standard diagnostic clinical interviews ranged from 3 percent to 9 percent across studies enrolling persons recruited from school or community-based settings^{170, 189, 223, 235} and was 11 percent in all three of the studies enrolling persons from nonpsychiatric clinical settings.^{172, 199, 219}

Two studies evaluated the original BDI;^{170, 235} the BDI-II published in 1996 was a substantial revision to the original BDI. Both studies reported sensitivity and specificity at a score threshold of 11 or higher (scores less than 9 are considered no or minimal depression, scores between 10 and 18 are considered "mild to moderate" depression²⁷² in adults). At a score threshold of 11, the sensitivity and specificity were 0.84 and 0.81, respectively, in one study^{219, 235} and 0.90 and 0.86,

respectively, in the other study. ¹⁷⁰ One of these studies also provided estimates of sensitivity and specificity at lower and higher thresholds (**Table 3**). ¹⁷⁰

Two studies evaluated the CES-D but did not evaluate the same thresholds. ^{189, 235} On this instrument, a score of 16 or more is considered positive for subthreshold depression in adults. ²⁷³ In one study, the sensitivity and specificity of a threshold score of 24 or more were 0.84 and 0.75, respectively. ²³⁵ The other study reported sensitivity and specificity separately for boys and girls at four different scoring thresholds (12, 16, 20, and 22). At the threshold of 16, the sensitivity in boys was 0.59 and in girls was 0.83, and the specificity in boys was 0.66 and in girls was 0.53. ¹⁸⁹

The CIS-R,²²³ HSCL,¹⁷² PHQ-A,¹⁹⁹ PI-ED,²¹⁹ and WHO-5¹⁷² were each only evaluated in one study. Across these instruments, the reported sensitivity ranged from 0.18 to 0.94, and the specificity ranged from 0.80 to 0.97. The outlier values were for CIS-R (reported sensitivity of 0.18 and specificity of 0.97, from analysis weighting for selection into the second phase of the study).²²³ Calculated sensitivity without weighting resulted in a sensitivity of 0.74 and specificity of 0.78.²²³

Based on the reported sensitivity and specificity data, the number of false-negatives and false-positives per 1,000 screening tests at the lowest $(3\%)^{235}$ and highest $(11\%)^{172, 219}$ prevalences reported in the included studies are reported in **Table 3**. For nearly all studies, the number of false-negatives is lower than the number of false-positives.

Results: Findings for Specific Populations

Subgroup Analyses

One study reported accuracy results separately for boys and girls for the CES-D instrument. ¹⁸⁹ The area AUC in boys was 0.61 and in girls was 0.77. Except for the lowest score threshold evaluated (greater than or equal to 12), the sensitivity in boys was markedly lower than in girls. The specificity at all four thresholds evaluated was higher in boys than in girls. Authors did not conduct formal statistical significance testing of these differences by sex.

The only study enrolling both children and adolescents did not report results separately by age.²¹⁹ No studies reported results by any other specific populations prespecified in our research plan.

Findings Within Age Groups

Only one study, as noted above, enrolled children along with adolescents and did not report the results by age. ¹⁸⁹ All other studies were restricted to adolescents.

Anxiety or Depression

Two fair-quality studies reported the accuracy of a positive screening test for either or both anxiety or depression diagnoses. ^{219, 234} One study reported on the sensitivity and specificity of the

PI-ED for either GAD or MDD,²¹⁹ and the other study reported on the accuracy of the 5-item Mental Health Index (MHI-5) for anxiety or depression.²³⁴

Study Characteristics

Authors conducted the study evaluating the PI-ED among youth ages 8 to 17 years (mean age 12 years) recruited from eight hospital outpatient pediatric departments in Scotland and from child and adolescent mental health clinics or psychology services. Nearly half (48%) were female, and nearly all were White. The-PI-ED test (score threshold of 20 or higher) was compared with the Computerized Diagnostic Schedule for Children, a type of structured clinical interview. Authors conducted the study evaluating the MHI-5 among youth ages 10 to 15 years (mean age 12 years) recruited from schools in Spain, and nearly half were female (49%). Authors evaluated both the full 5-item MHI-5 instrument and also the 3-item "distress" factor; the 2-item well-being factor was not evaluated. The MHI-5 screener was also compared with a structured clinical interview (Anxiety Disorders Interview Schedule for DSM-IV: Child and Parent Version).

Results of Included Studies

The sensitivity and specificity of the PI-ED for either a diagnosis of GAD, MDD, or both at a score threshold of 20 was 0.83 and 0.93, respectively. The AUC for the full MHI-5 instrument for anxiety or depression was 0.78 (95% CI, 0.64 to 0.93). The authors reported that the optimal threshold was a score of 3 or higher on the 3-item distress factor of the full MHI-5, which yielded a sensitivity of 0.69 and a specificity of 0.72 (AUC 0.80; 95% CI, 0.68 to 0.92 for the 3-item distress factor). ²³⁴

Results: Findings for Specific Populations

Subgroup Analyses

Authors reported no results by specific populations of interest prespecified for this update.

Findings Within Age Groups

Both studies included children and adolescents; neither reported on children and adolescents separately.

KQ 3. What Are the Harms Associated With Screening for Depression, Anxiety, or Suicide Risk in Primary Care or Comparable Settings in Children and Adolescents?

Suicide Risk

Summary

We included two RCTs of fair quality (described in 2 articles). ^{267, 268} Neither study is new to this update. Detailed study, population, intervention characteristics, and results are provided in **Appendix I Table 2 through Table 4**.

Study Characteristics

We identified two fair-quality trials (total randomized N=2,675) conducted in high school settings relevant to this KQ.^{267, 268} Both studies randomly assigned students to complete items relating to suicidal ideation and behaviors as part of an assessment of universal mental health screening²⁶⁷ or as part of larger questionnaires concerning the evaluation of a workshop.²⁶⁸ In the universal screening study (N=2,342), half of the classrooms in six high schools located in Nassau, Suffolk, and Westchester counties (New York State) were randomized to receive the suicide questions on the first day (intervention group), and the other half received them on the second day (control group).²⁶⁷ In the workshop evaluation study (N=333), half of the students in Year 10 at a single all-boys school in Melbourne, Australia, were randomized to receive the suicide items on the first day (intervention group), while the others received them on the second day (control group).²⁶⁸ Both studies compared measures of distress between Day 1 screened and Day 2 students to assess the impact of screening for suicidal risk.

Results

The universal screening study reported no differences in distress immediately after the screening questionnaire or in persistent distress (measured 2 days later) between the intervention and control groups as measured by the adolescent version of the Profile of Mood States (POMS-A).²⁶⁷ POMS-A is designed to capture transient mood states and is sensitive to change over short periods of time; detailed POMS-A results are reported in Appendix I Table 4.²⁶⁷ Similarly, a workshop evaluation study reported no significant difference in five of the six POMS-A subscales.²⁶⁸ One subscale (vigor) was significantly different between groups, but this may be due to chance.²⁶⁸

The universal screening measured suicidal ideation in both groups on the Day 2 survey and found no significant differences between groups (mean score 6.5 [standard deviation (SD): 11.5] vs. 6.2 [10.5], p=0.86) as measured by the Suicidal Ideation Questionnaire-Junior (SIQ-JR) instrument on the rates of participants with suicidal ideation between the first and second surveys (4.7% vs. 3.9%, p=0.49).²⁶⁷ These results suggest that exposure to the suicide screening items on Day 1 in the intervention group did not result in any increases in suicidal ideation.²⁶⁷

In the workshop evaluation study, authors asked students about their level of distress in answering questions about self-harm and suicide after both groups had answered the suicide screening items: 5.2 percent reported that it was "moderately distressing" and 3.7 percent reported that it was "very distressing." Fifty percent reported that it was "not at all distressing." ²⁶⁸

Neither study examined screening-related harms by sex, race, or ethnicity.

Depression

We did not identify any studies reporting on harms of screening for depression.

Anxiety

We did not identify any studies reporting on harms of screening for anxiety.

Anxiety or Depression

We did not identify any studies reporting on harms of screening in populations with anxiety or depression.

KQ 4. Does Treatment (Psychotherapy, Pharmacotherapy, or Collaborative Care) of Depression, Anxiety, or Suicide Risk Result in Improved Health Outcomes in Children and Adolescents?

Suicide Risk

Summary

We included 16 RCTs of good or fair quality (described in 23 articles). ^{164, 179-182, 191-194, 197, 200-202, 212-215, 221, 222, 229, 236, 245, 265} Nine of these studies are new to this update. ^{164, 179-181, 192, 194, 202, 212-215, 221, 222, 229, 236} Detailed study, population, intervention characteristics, and results are provided in **Appendix I Table 5 through Table 16**. Detailed outcomes included in meta-analyses are provided in **Appendix F Table 1 and Table 2**. Meta-analysis forest plots are provided in **Appendix G Figure 1 through Figure 7**.

Study Characteristics

The characteristics of the included studies are summarized in **Table 4**. Fourteen studies admitted children based on elevated suicide risk, $^{164, 179-181, 191-194, 197, 200-202, 212-215, 221, 222, 229, 236, 265}$ and two studies admitted children with suicide risk and self-reported depressive symptoms (BDI> 19245) or BDI> 20182).

Mean ages ranged from 14 to 18 years. All 16 included studies focused on adolescents (ages 11 to 19 years) $^{164, 179-182, 191-194, 197, 200-202, 212-215, 221, 222, 229, 236, 245, 265}$ and included a majority of female participants. Ten studies reported a majority of White participants, $^{164, 191, 192, 194, 197, 200-202, 221, 222, 229, 236}$ one study included a majority of African American participants, 182 and five studies did not report race or ethnicity. $^{179-181, 193, 212, 245, 265}$

All included studies examined psychotherapy, counseling, support, or a combination with variable intensity and duration. Fifteen studies compared these interventions with treatment as usual (TAU), ^{164, 179-182, 191-193, 197, 200-202, 212-215, 221, 222, 229, 236, 245, 265} and one study compared intervention to attention control. ¹⁹⁴ Fifteen of the included trials ^{164, 179-182, 191-194, 200-202, 212-215, 221, ^{222, 229, 236, 245, 265} examined one active arm, and one trial ¹⁹⁴ examined three active treatment arms. Five trials included individual child-/adolescent-only interventions, ^{194, 197, 202, 221, 222, 245} three included child-/adolescent-only group-based interventions, ¹⁹¹⁻¹⁹³ one included family-based intervention, ¹⁷⁹⁻¹⁸¹ three included caregiver-/supporting adult–only interventions, ^{197, 200, 201, 229} and six included a combination of individual child-/adolescent-, caregiver-/supporting adult-, group-, or family-based interventions. ^{164, 182, 197, 212-215, 236, 265} Duration of treatment ranged between one single session to weekly sessions over 12 months. Overall, 11 trials ^{164, 179-182, 191-193, 212-215, 229, 236, 245, 265} examined interventions that required 3 or more sessions), and five trials ^{194, 197, 200-202, 221, 222} examined interventions requiring fewer than 3 sessions). No evidence was captured that examined pharmacotherapies.}

All 16 studies reported on suicide or self-harm—related outcomes, 13 studies reported on depression, ^{179-182, 191-194, 197, 200, 202, 212-215, 236, 245, 265} three studies reported on anxiety, ^{192, 197, 245} one trial reported on burdensomeness, ¹⁹⁴ eight studies reported on functioning, ^{179-181, 191, 193, 200, 212-215, 221, 222, 229, 265} two studies reported on response, ^{182, 194} and one study reported on all-cause mortality. ²⁰¹ Time of measurement across all outcomes ranged from 2 weeks to 14 years.

Two studies recruited participants from schools; ^{197, 245} five recruited from child and adolescent mental health services; one recruited from emergency departments and community mental health services; ²²⁹ two recruited from emergency departments and child and adolescent mental health services; ^{221, 222, 236} one recruited from emergency departments and primary care offices; ¹⁸² one recruited from emergency departments, inpatient/patient hospitalization, and outpatient services; ¹⁶⁴ one recruited solely from a hospital emergency department; ²⁰² one recruited from psychiatric outpatient clinics; ^{181, 212-215} one recruited participants from schools and public gathering places frequented by adolescents; ¹⁹⁴ and one study recruited participants from inpatient settings following psychiatric hospitalization. ^{200, 201}

Included studies were conducted in the United States, ^{164, 182, 194, 197, 200-202} United Kingdom, ^{179-181, 191, 192, 221, 222, 236, 265} Australia, ^{193, 229} Norway, ^{181, 212-215} and Taiwan. ²⁴⁵ Six of the included studies ^{179-181, 191, 193, 194, 212-215, 265} were rated as good quality, and 10 studies ^{164, 182, 192, 197, 200-202, 221, 222, 229, 236, 245} were rated fair quality. Two of the included studies reported on specific populations of interest. ¹⁷⁹⁻¹⁸²

Results: Suicide Deaths

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Three studies reported on the effects of suicide or self-harm interventions with variable intensity and duration on suicide deaths at the end of treatment (19 weeks to 12 months). ^{191, 200, 212-215} Studies compared dialectical behavior therapy (DBT), ²¹²⁻²¹⁵ youth-nominated support team, ²⁰⁰ or group therapy with TAU. Two of the interventions ^{191, 212-215} were high contact (>3 sessions), and one intervention ²⁰⁰ was low contact (<3 sessions). Two studies ^{191, 212-215} reported no suicide deaths at the end of treatment in either arm. One study, using a youth-nominated support team approach (n=346) reported no statistically significant differences between intervention and control at the end of treatment (0 vs. 1, p=NR). ²⁰⁰ A longer term followup of that study, 11 to 14 years after psychiatric hospitalization for suicide risk (baseline for the study), found no statistically significant differences in suicide-related deaths. ²⁰¹ One study of DBT continued to record no deaths in either arm at the 3-year followup. ²¹²⁻²¹⁵

Results: Suicide-Related Hospitalization or Emergency Department Use

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Five studies reported on the effects of suicide or self-harm interventions with variable intensity and duration on suicide-related hospitalization or emergency department use at the end of treatment (12 weeks to 2 years) (**Appendix F Table 1**). ^{164, 179-181, 192, 212-215, 221, 222} Four studies reported nonsignificant differences between intervention and TAU, and one study ¹⁶⁴ reported significant differences. Included studies examined family therapy, ¹⁷⁹⁻¹⁸¹ DBT, ²¹²⁻²¹⁵ therapeutic assessment, ^{221, 222} mentalization-based therapy (MBT) ¹⁹², and CBT. ¹⁶⁴ Four of the interventions ^{164, 192, 212-215} were high contact (≥3 sessions), and one intervention ^{221, 222} was low contact (<3 sessions).

Results were pooled for the three studies reporting on use of hospitals or emergency departments: hospital attendance for self-harm, ¹⁷⁹⁻¹⁸¹ self-harm presentation to accident and emergency department, ^{221, 222} or self-harm presentation to emergency department. ²¹²⁻²¹⁵ These studies resulted in a pooled RR of 0.998 (**Appendix G Figure 1**, 95% CI, 0.67 to 1.50; N=978; k=3; *I*²=21%; p=0.28). One study did not report sufficient data to permit pooling and reported no statistically significant differences in the mean number of self-harm emergency department presentations between MBT and TAU (0.36 vs. 0.23, p=NR). ¹⁹² A fifth study ¹⁶⁴ reported significant differences between intervention and TAU; the study reported that the probability of survival at 3-month post-treatment without an emergency department visit for suicidality was lower for the TAU group (0.71, SE 0.11) compared with CBT (0.90, SE 0.07, Z=2.00, p=0.045, number needed to treat=5.26); in sensitivity analyses, these differences were no longer statistically significant. The differences for hospitalization were not statistically significantly different.

The study reporting on self-harm presentation to emergency departments also reported on hospital admissions due to self-harm and found no statistically significant differences between DBT and TAU (2% vs. 5%, p=NS). $^{212-215}$

One study reported on hospital attendance for self-harm event at 12 months, 18 months, and 36 months and continued to find no statistically significant differences between family therapy and TAU. ¹⁷⁹⁻¹⁸¹ One study of MBT continued to report no statistically significant differences between arms in mean number of self-harm emergency department presentations at 24 weeks. ¹⁹²

Results: Suicide Attempts or Episode of Deliberate Self-Harm

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Nine studies reported on the effects of suicide or self-harm interventions with variable intensity and duration on suicide attempts or episodes of deliberate self-harm at the end of treatment (0 to 36 months). ^{164, 179-181, 191-193, 200, 212-215, 236, 265} Included studies compared DBT-informed CBT, ¹⁶⁴ family therapy, ¹⁷⁹⁻¹⁸¹ group psychotherapy, ^{191, 193} MBT, ¹⁹² youth-nominated support team, ²⁰⁰ DBT, ²¹²⁻²¹⁵ mentalization-based treatment, ²³⁶ or developmental group therapy ²⁶⁵ with TAU. Eight of the interventions ^{164, 179-181, 191-193, 212-215, 236, 265} were high contact (>3 sessions), and one intervention ²⁰⁰ was low contact (<3 sessions). Studies reported on a variety of outcomes including mean number of self-harm events, ^{179-181, 212-215, 265} number of self-harm events, ^{179-181, 191, 193, 236, 265} number of suicide attempts, ²⁰⁰ frequency of self-harm, ¹⁹¹ severity of self-harm, ¹⁹¹ Risk-Taking and Self-Harm Inventory for Adolescents (RTSHI), ^{192, 236} nonsuicidal self-injury, ¹⁶⁴ and percentage with suicide ideation. ¹⁶⁴ Study sample sizes ranged from 42 to 832. The most commonly reported measures were mean number of self-harm events and number of self-harm events. The detailed results of the included studies are summarized in **Appendix F Table 1**.

Table 5 presents pooled estimates of effect for end-of-treatment measures, specifically mean number of self-harm events (3 studies)^{179-181, 212-215, 265} and proportion of self-harm events (5 studies).^{179-181, 191, 193, 236, 265} Both estimates of effect were not statistically significant and had wide confidence intervals. One study, included in the meta-analysis of posttreatment results, continued to report statistically nonsignificant differences in number of self-harm events between arms at the 1-year. At the 3-year followup, unadjusted analyses favored the intervention. After adjustment for variables used in stratification at randomization (gender, presence of depressive disorder at the time of randomization, and having had at least one suicide attempt within the last 4 months), the differences were no longer statistically significant.²¹²⁻²¹⁵

Five studies ^{164, 191, 192, 200, 265} reported on other suicide attempt or deliberate self-harm outcomes (number of suicide attempts, frequency of self-harm, severity of self-harm, number of persons repeating self-harm, nonsuicidal self-injury, percentage with suicide ideation, and RTSHI) posttreatment (0 to 12 months). Included studies compared DBT-informed CBT, ¹⁶⁴ group psychotherapy, ¹⁹¹ MBT, ¹⁹² youth-nominated support team, ²⁰⁰ or developmental group therapy ²⁶⁵ with TAU. Four of the interventions ^{164, 191, 192, 265} were high contact (>3 sessions), and one intervention ²⁰⁰ was low contact (<3 sessions). These results did not consistently demonstrate statistically significant differences favoring the intervention arm. Studies reported significant

differences between intervention and TAU on the outcomes of number of persons repeating self-harm (6% vs. 32%; OR, 6.3 [95% CI, 1.4 to 28.7]),²⁶⁵ percentage with suicide ideation (0% vs. 18.2%; p=0.01),¹⁶⁴ and nonsuicidal self-injury (estimated probabilities of survival without: 0.55 vs. 0.43; p=0.05).¹⁶⁴ No statistically significant differences were reported when the intervention was compared with TAU on the number of suicide attempts,²⁰⁰ frequency of self-harm,¹⁹¹ severity of self-harm,¹⁹¹ and RTSHI scores.¹⁹² A study of group psychotherapy continued to report no statistically significant differences in frequency and severity of self-harm between arms at 6 to 12 months.¹⁹¹ A study of MBT continued to report no statistically significant differences in RTSHI total score and RTSHI self-harm subscales between arms at 24 and 36 weeks.¹⁹²

Results: Suicidal Ideation

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Twelve studies reported on the effects of suicide or self-harm interventions with variable intensity and duration on measures of suicide risk. ^{179-182, 191, 193, 194, 197, 200, 202, 212-215, 236, 245, 265} Included studies compared family therapy, ¹⁷⁹⁻¹⁸¹ attachment-based therapy, ¹⁸² group psychotherapy, ^{191, 193} youth-nominated support team, ²⁰⁰ motivational interviewing, ²⁰² DBT, ²¹²⁻²¹⁵ MBT, ²³⁶ intensive interpersonal psychotherapy for depressed adolescents with suicidal risk (IPT-A-IN), ²⁴⁵ internet-based CBT, ¹⁹⁴ child interview with counseling, ¹⁹⁷ parent sessions, ¹⁹⁷ child interview with counseling plus parent sessions, ¹⁹⁷ or developmental group therapy. ²⁶⁵ Eight of the interventions ^{179-182, 191, 193, 212-215, 236, 245, 265} were high contact (>3 sessions), and four interventions ^{194, 197, 200, 202} were low contact (<3 sessions). Eleven studies compared intervention with TAU, ^{179-182, 191, 193, 197, 200, 202, 212-215, 236, 245, 265} and one study compared intervention with attention control. ¹⁹⁴ Studies reported on a variety of measures including the Beck Scale for Suicide Ideation (BSS), Beck Hopelessness Scale (BHS), Suicidal Ideation Questionnaire (SIQ), SIQ-JR, Hopelessness Scale for Children (HSFC), Scale for Suicidal Ideation (SSI), Adolescent Suicide Questionnaire—Revised (ASQ-R), burdensomeness, and individual suicide risk indicators. Study sample sizes ranged from 48 to 832. The detailed results of the included studies are summarized in **Appendix F Table 2**.

The most commonly reported measures were the BHS, SIQ-JR, and SIQ. **Table 6** presents pooled estimates for these measures. Our studies^{200, 202, 212-215, 245} reported on the BHS at the end of treatment (2 months to 19 weeks).

Seven studies^{182, 191, 193, 200, 202, 212-215, 265} reported on the SIQ or SIQ-JR at the end of treatment (2 months to 7 months). The pooled estimate for the BHS was statistically significant and favored treatment arms when compared with controls. The pooled estimate and results from individual studies for the SIQ/SIQ-J, however, favored treatment arms, but the confidence intervals spanned the null.

Regarding longer term outcomes, findings were mixed. Two studies reporting nonsignificant differences on the BHS at 6 weeks and 19 weeks posttreatment continued to report nonsignificant differences on the BHS at additional follow-ups ranging between 3 months and 3.1 years. ^{200, 212-215} One study of attachment-based family therapy continued to find statistically

significant differences favoring the intervention arm on the SIQ-JR between arms at 24 weeks. ¹⁸² One study of youth-nominated support team continued not to find statistically significant differences on the SIQ-JR between study arms at 3 months or 12 month. ²⁰⁰ One study of DBT continued not to find any significant difference between study arms on the SIQ-JR at 3.1 years. ²¹²⁻²¹⁵ A study of group psychotherapy ¹⁹¹ and a study of group therapy ¹⁹³ both continued not to find statistically significant differences on the SIQ at 12 months.

Six studies^{179-182, 194, 197, 229, 245} reported on other suicide risk measures (ASQ-R, BSS, HSFC, SSI, individual suicide risk indicators) at the end of treatment (2 weeks to 12 months) that we could not pool because studies used heterogeneous measures or were not sufficient to pool.

Three studies reported on the BSS at the end of treatment, but the specific measures could not be pooled. ^{179-181, 194, 245} Specifically, one study reported that a smaller proportion of participants in family therapy reported suicide ideation based on the BSS compared with TAU at the end of treatment (OR, 0.64 [95% CI, 0.44 to 0.94]; p=0.024), but no statistically significant differences were reported at the 18-month followup (OR, 0.76 [95% CI, 0.49 to 1.16]; p=0.20). ¹⁷⁹⁻¹⁸¹ Two additional studies reported continuous measures of the BSS and found inconsistent results. One reported a statistically significant difference between the IPT-A-IN and TAU at the end of treatment (6 weeks, 8.73 vs. 11.89; p=0.05), ²⁴⁵ and one reported no statistically significant differences between internet CBT and information-only control at the end of treatment (2.05 vs. 4.49, p=0.12) and at the 8-week followup (1.69 vs. 2.57; p=0.92). ¹⁹⁴

Results from other single studies on the ASQ-Jr, HSFC, SSI, and individual suicide risk indicators generally demonstrated at least some statistically significant benefit for suicide risk intervention. ^{182, 197, 229} The only exception was one study that found no differences on the HSFC, but the same study found significantly lower odds of suicidal ideation using the BSS, as noted above. ¹⁷⁹⁻¹⁸¹

One study¹⁹⁴ reported on the effects of suicide or self-harm intervention on perceived burdensomeness at the end of treatment (2 weeks) and 8 weeks posttreatment. The study compared internet CBT with information-only control. The study reported no statistically significant differences in mean perceived burdensomeness scores between internet CBT and information control at posttreatment (17.76 vs. 18.81, p=0.26) or at 8 weeks posttreatment (13.90 vs. 15.8; p=0.10).

Results: Response, Remission, and Loss of Diagnosis

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Two studies reported on the effects of suicide or self-harm intervention on clinical response at the end of treatment (8 to 12 weeks). $^{182, 194}$ One study compared attachment-based therapy to enhanced usual care and reported statistically significant differences between groups, favoring intervention. 182 The study reported greater clinical response in the intervention group compared with TAU based on SIQ-JR scores (defined as \leq 13) at the end of treatment and 24 weeks posttreatment (12 weeks: 87% vs. 52%, OR, 6.30 [95% CI, 1.76 to 22.61]; 24 weeks: OR, 4.41;

p=0.008). The study also reported that intervention was associated with greater clinical response based on SSI scores (defined as 0 vs. 1 suicide attempt) at the end of treatment and at the 24-week followup (12 weeks: 69% vs. 35%, OR, 4.45 [95% CI, 1.33 to 13.56]; 24 weeks: OR, 5.37 [95% CI, 1.56 to 18.48], p=0.006). A second study comparing internet CBT to information-only control reported no statistically significant differences in response (defined as perceived burdensomeness <14.61) between groups (24% vs. 10%, calculated OR, 2.82 [95% CI, 0.80 to 9.91]) at the end of treatment (8 weeks). 194

Results: All-Cause Mortality

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

A long-term followup of a study on a youth-nominated support team approach,²⁰⁰ 11 to 14 years after psychiatric hospitalization for suicide risk (baseline for the study), found a higher number of deaths in the National Death Index in the treatment as usual group when compared with the active treatment group (13/225 vs. 2/223; hazard ratio: 6.62 [95% CI, 1.49 to 29.35]).²⁰¹ The National Death Index can under-ascertain deaths.²⁷⁴ The same study did not demonstrate an effect on the primary outcome of suicidal ideation; as a result, findings by chance or through other mechanisms of action (such as improved problem solving) cannot be ruled out.

Results: Functioning

Psychotherapy, Counseling, Support, or Combined Interventions vs. Treatment as Usual or Attention Control

Eight studies reported on the effects of suicide or self-harm interventions compared with TAU on functioning outcomes in adolescents. ^{179-181, 191, 193, 200, 212-215, 221, 222, 229, 265} **Table 7** presents pooled estimates of effect for end-of-treatment outcomes on the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA) ^{191, 193, 229, 265} and Children's Global Assessment Scale (CGAS). ^{193, 213, 222} Both estimates of effect found no statistically significant differences in functioning and had wide confidence intervals spanning the null.

Regarding longer term outcomes, one study²²⁹ included the meta-analysis for HoNOSCA and demonstrated a statistically significant improvement in functioning favoring at the intervention group posttreatment also found statistically significant differences favoring the intervention group at the 6-month followup (M [SD]=4.77 [4.45] vs. 12.72 [5.29], p<.01).

Three studies reporting on other measures of functioning including the Child and Adolescent Functional Assessment Scale (CAFAS), ²⁰⁰ General Health Questionnaire (GHQ), ¹⁸⁰ Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES), ¹⁸⁰ and Strengths and Difficulties Questionnaire (SDQ), ¹⁹³ reported nonsignificant differences in functioning outcomes at posttreatment and followup.

Results: Findings for Specific Populations

Subgroup Analyses

Findings for specific populations are reported in **Appendix I Table 15**. No studies reported results by race/ethnicity, sexual identity, or gender orientation. One study¹⁷⁹ comparing family therapy (N=415) with TAU (N=417) reported nonsignificant differences in hospital attendances for self-harm events as a function of age (chi-square: 0.4730, p=0.49) or sex (chi-square: 1.5219, p=0.2173).

Findings Within Age Groups

All studies reported results for adolescent participants.

Anxiety

Summary

As noted previously, we limited the synthesis to CBT for psychotherapy; we included pharmacotherapies approved by the FDA for children and adolescents. We included 29 RCTs (described in 40 articles) of good or fair quality. ^{163, 165, 167-169, 177, 178, 183, 190, 195, 196, 198, 203, 206, 220, 224-228, 237-244, 246, 251, 253-262} All studies are new to this report because this topic has not been addressed previously by the Task Force. Detailed study, population, intervention characteristics, and results are provided in **Appendix I Tables 17 through 22**. Detailed outcomes are provided in **Appendix F Table 3 through Table 11**. Meta-analysis forest plots are provided in **Appendix G Figure 8 through Figure 24**.

Study Characteristics

The characteristics of the included trials are summarized in **Table 8**. Sixteen studies enrolled children with any anxiety disorder to the trial. ^{163, 167, 168, 177, 183, 190, 195, 198, 203, 206, 237, 241, 242, 246, 251, 253} The most common primary diagnoses in these studies were social anxiety disorder and GAD. Of the studies requiring specific anxiety disorders for trial eligibility, five required GAD, ^{196, 224, 238, 243, 244} four required social anxiety disorder, ^{165, 220, 239, 240} two required selective mutism, ^{169, 178} and two required either GAD, social anxiety disorder, or separation anxiety. ^{225-228, 254-262} Nine studies set a threshold for severity, ranging from requiring clinically important symptoms or functional impairment to specific minimum thresholds on the Clinical Global Impressions-Severity (CGI-S), Pediatric Anxiety Rating Scale (PARS), or anxiety disorders interview schedule for DSM-IV for Children-Children/Parents (ADIS-C/P) clinician severity ratings (CSR). ^{168, 196, 220, 225-227, 237, 238, 243, 251}

The mean age of enrolled populations ranged from 4.1 to 17.4 years. Three studies focused on early childhood (ages 3 to 7 years), ^{183, 195, 237} 11 focused on later childhood (ages 6 to 14 years), ^{165, 167, 178, 196, 203, 206, 220, 240, 241, 246, 251} 11 spanned childhood and adolescence, ^{163, 168, 169, 177, 190, 198, 224-228, 238, 243, 254-262} and four focused solely on adolescence. ^{239, 242, 244, 253} Nine of 29 studies had a majority of male participants. ^{167, 203, 206, 225-228, 237, 238, 246, 251}

Nineteen of 29 studies provided information about the race or ethnicity of enrolled populations. With the exception of one study with all Japanese participants (set in Japan). ¹⁹⁸ White participants were a majority in all studies. ^{168, 177, 178, 190, 195, 206, 224-228, 237, 238, 241, 243, 244, 246, 251, 253-262}

Pharmacotherapy trials, with one exception, ¹⁶⁹ used narrow inclusion criteria and excluded persons with other psychiatric conditions. In contrast, psychotherapy trials did not routinely exclude participants with other psychiatric conditions.

Half the studies advertised widely for recruitment. ^{165, 167, 168, 177, 178, 183, 190, 195, 196, 198, 203, 206, 239, 241, 242} A minority of studies relied solely on referrals from mental health professionals, ^{163, 220, 224-228, 237, 238, 244, 246, 251, 253} two were recruited entirely through schools, ^{169, 240} and two did not specify the clinical setting for recruitment. ^{243, 254-262} Ten studies recruited participants from the United States, ^{168, 169, 178, 190, 195, 225-228, 237, 238, 244, 254-262} and one drew from multiple countries, including the United States, Mexico, and South Africa, but had a majority of participants from the United States. ²⁴³ The other 19 studies recruited participants from other countries with a very high human development index, namely Australia, the United Kingdom, Denmark, Germany, Norway, Hong Kong, Japan, Spain, and Sweden.

With respect to interventions evaluated, 22 RCTs evaluated CBT, ^{163, 165, 167, 177, 178, 190, 195, 196, 198, 203, 206, 220, 224, 237, 239, 241, 242, 246, 251, 253 six evaluated pharmacotherapy, ^{168, 169, 225-228, 238, 243, 244} and one evaluated both CBT and pharmacotherapy and combinations of CBT and sertraline. ²⁵⁴⁻²⁶² As a reminder, psychological interventions in this review for the USPSTF were limited to CBT because it is the most commonly used intervention for anxiety disorders. Our search identified other types of psychological interventions used to treat anxiety disorders, and these are cataloged in **Appendix A**.}

The most commonly studied CBT intervention was individually directed CBT, and the most commonly studied pharmacotherapies were sertraline and fluoxetine. Typically, these interventions were compared with wait-list for CBT and placebo for pharmacotherapy.

For CBT, the duration of therapy ranged from 5 days for group CBT to 31 weeks for individual CBT. The modal duration was 12 weeks. Although trials commonly reported weekly therapy lasting for 30 to 90 minutes, the intensity of treatment could be as high as 5 consecutive days of six to eight hour-long sessions for a 5-day group CBT trial¹⁷⁸ or 25 individual 50-minute sessions for the 31-week therapy.²³⁹

Studies relied largely on in-person delivery of interventions; two studies reported on internet CBT. ^{242, 253}

Fourteen CBT studies reported results comparing a single treatment arm with wait-list control. ¹⁶³, ¹⁶⁵, ¹⁷⁷, ¹⁷⁸, ¹⁸³, ¹⁹⁵, ¹⁹⁶, ¹⁹⁸, ²⁰³, ²²⁴, ²³⁹, ²⁴¹, ²⁴², ²⁵³ Two CBT studies reported results comparing a single treatment arm with TAU in primary care settings. ¹⁹⁰, ²³⁷

For pharmacotherapy, the duration of treatment ranged from 8 to 12 weeks, with doses being adjusted either flexibly or in a preplanned manner during therapy. Two studies reported

concurrent psychoeducational therapy, ^{178, 225-228} and one reported medication therapy management visits. ²³⁸

Six pharmacotherapy studies compared fluoxetine, ^{168, 169} fluvoxamine, ²²⁵⁻²²⁸ sertraline, ²³⁸ escitalopram, ²⁴⁴ or duloxetine ²⁴³ with placebo.

Six studies had more than one active arm compared with wait-list control. ^{167, 206, 220, 240, 246, 251} Five had two arms comparing individual CBT versus group CBT, ²⁵¹ group CBT with and without cognitive restructuring, ²⁴⁰ brief CBT versus full CBT, ²⁴⁶ and child-focused CBT versus parent- or family-inclusive CBT. ^{167, 220} A sixth compared three variants of parent-guided CBT, supported by telephone, email, or as needed, against a wait-list control. ²⁰⁶

One had three active arms compared with placebo or wait-list control. This study (Child/Adolescent Anxiety Multimodal Study, or CAMS) evaluated CBT, sertraline, and CBT plus sertraline versus placebo. ²⁵⁴⁻²⁶²

All studies reported on continuous or categorical outcome measures for anxiety symptoms, and nearly all studies (except three) reported on response, remission, or loss of diagnosis. Nine studies reported on depression outcomes, and fourteen on functioning. Studies generally reported results at the end of treatment, with the timing ranging from 4 weeks to 6 months; a minority reported results at 12 months. 190, 220

Six studies reported on analyses of specific populations. 167, 190, 241

Results: Anxiety Symptoms

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

All 24 CBT studies reported on anxiety symptoms. Studies did not report minimal clinically important differences, but scores above established thresholds indicated clinical benefit and are presented in **Table 9** for pooled estimates. All outcomes for each study are reported in **Appendix** F Table 3 and these were used to generate meta-analyses (Appendix G Figure 8 through Figure 14). Table 9 presents pooled estimates of effect for end-of-treatment measures, specifically ADIS CSR (12 studies 163, 177, 178, 183, 196, 198, 206, 224, 237, 242, 253, 275); child-rated Spence Children's Anxiety Scale (SCAS) (9 studies 163, 177, 196, 198, 203, 206, 242, 246, 253); parent-rated SCAS (9 studies 163, 177, 196, 198, 203, 206, 242, 246, 253); child-rated SPAI (4 studies 165, 220, 239, 240, 275); CGI-S (3 studies 190, 237, 254-262); Multidimensional Anxiety Scale for Children (MASC) (3 studies 220, 251, 254-^{262, 275}); and Revised Children's Manifest Anxiety Scale (RCMAS) (3 studies ^{167, 206, 241}). Results for nearly all measures suggested clinically and statistically significant differences favoring CBT over wait-list control, TAU in primary care, or placebo. The only exceptions was for MASC (3 studies^{220, 251, 254-262, 275}). Studies reporting parent- and child-rated MASC outcomes did not consistently show statistically significant differences favoring CBT over wait-list control or placebo. Studies reporting on MASC did not offer a threshold for clinically meaningful effect, and an evaluation of MASC suggests that it may not be possible to identify cutoff scores.²⁷⁶

In addition, we found results for several posttreatment measures that we could not pool, either because of heterogeneity in measures or because we found only one or two studies. Heterogenous measures included child-reported SCARED outcomes. measured at 10 to 12 weeks from baseline. ^{190, 224, 254-262} One study reported on subscales for SCARED for GAD and anxiety²²⁴ rather than total scores, and the details regarding the scale and scoring were unclear. Studies reporting parent- and child-rated SCARED outcomes did not consistently show statistically significant differences favoring CBT over wait-list control.

We found one or two studies on several other symptom measures, specifically two studies each on the Fear Survey Schedule for Children-Revised (FSCC-R), ^{167, 220} Social Anxiety Scale Children (SASC), ^{165, 240} and PARS^{237, 254} and one study each on parent-reported Social Phobia and Anxiety Inventory (SPAI), ^{220, 275} Liebowitz Social Anxiety Scale for Children and Adolescents (LSAS-CA), ²³⁹ Preschool Anxiety Scale (PAS), ¹⁸³ Penn State Worry Questionnaire for Children (PSWQ-C), ²²⁴ Selective Mutism Questionnaire (SMQ), ¹⁷⁸ CGI-I, ¹⁹⁵ and Diagnostic Interview Schedule for Children, Adolescents, and Parents (DISCAP). ²⁴¹ With the exception of one study, ¹⁶⁷ all reported at least one measure favoring CBT compared with wait-list control or placebo for anxiety symptoms.

Three studies reported on outcomes after the initial posttreatment assessment, at 6 and 12 months, using three different instruments. The results were mixed. One study reported on childrated SPAI outcomes at 6 months and found statistically significant differences favoring CBT. Two studies reported no statistically significant differences at 12 months using CGI-S outcomes and SCARED. The studies reported no statistically significant differences at 12 months using CGI-S outcomes and SCARED.

Pharmacotherapy vs. Placebo

Six studies reported on the effects of pharmacotherapy on anxiety symptoms when compared with placebo (one each on duloxetine, ²⁴³ escitalopram, ²⁴⁴ fluoxetine, ¹⁶⁸ and fluvoxamine ²²⁵⁻²²⁸ and two on sertraline ^{238, 254-262}) (**Appendix F Table 4**). The studies enrolled persons with any anxiety disorder ^{168, 225-228} or specifically persons with GAD. ^{238, 243, 244} These studies reported on outcomes at the end of treatment using a variety of instruments, including the PARS, CGI-S, ADIS, RCMAS, SCARED, and MASC. Pooled estimates of effect for the PARS ^{168, 225-228, 243, 244, 254-262} and CGI-S (4 studies ^{238, 243, 244, 254-262}) suggested clinically and statistically significant improvement for both measures (**Table 9**). One or two studies reported findings for other measures (proportion with CGI-S less than 4; continuous measures of the CGI-I, SCARED-C, SCARED-P, child-rated MASC, parent-rated MASC, RCMAS, Hamilton Anxiety Rating Scale [HAM-A], and ADIS-CSR), ^{168, 238, 254-262} precluding pooling the results. In all but one instance, ²⁵⁵ studies reported statistically significant differences favoring pharmacotherapy.

Combination Therapy (Sertraline Plus CBT) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. ²⁵⁴⁻²⁶² The study reported on multiple measures of symptoms including the PARS, ²⁵⁴ CGI-S, ²⁵⁴ child-rated MASC, ²⁵⁵ parent-rated MASC, ²⁵⁵ SCARED-C, ²⁵⁵ and SCARED-P. ²⁵⁵ Results varied by instrument and respondent. PARS scores were significantly different favoring combination treatment at 12 weeks (calculated mean difference: -5.20 [95% CI, -6.91 to -3.50]²⁵⁴), but not

when evaluating changes from baseline to 12 weeks. Scores for the CGI-S (calculated mean difference: -1.4 [95% CI, -1.77 to -1.03]²⁵⁴) and parent-reported MASC (33.4 vs. 49.1, adjusted p<0.001) suggested benefit for the combined therapy arm when compared with placebo.²⁵⁵ Results for SCARED (9.6 vs. 19.5, adjusted p<0.001)²⁵⁵ were statistically significant and favored combination therapy, but child-reported measures of the MASC and SCARED did not yield statistically significant differences between treatment and control groups.

Results: Response, Remission, or Loss of Anxiety Diagnosis

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

Eight studies reported on clinical response, ^{178, 190, 195, 237-239, 242, 244, 253-262} seven on remission of anxiety symptoms, ^{163, 198, 206, 237, 239, 242, 254-262} and 19 on loss of diagnosis. **Table 10** presents pooled results for these outcomes; detailed outcomes are in **Appendix F Table 5 through Table 7**.

Of the eight studies reporting measures of clinical response, ^{178, 190, 195, 237-239, 242, 244, 253-262} six reported CGI-I response defined as moderately or markedly improved symptoms at the end of treatment, with outcomes measured at 4 weeks to 6 months from baseline (CGI-I score of 1 or 2); ^{178, 190, 195, 237, 254} the pooled RR was 1.89 (**Appendix G Figure 17,** 95% CI, 1.17 to 3.05; N=606; k=6; *I*²=64%). A seventh study defined response as reduction in the LSAS-CA total score of 31 percent or more. ²³⁹ The study reported statistically significant differences favoring CBT (66% vs. 20%, p=0.006). The eighth study defined response as a clinically reliable change in SCAS scores. ²⁴² The study reported statistically significant differences favoring CBT on the child-reported SCAS (69% vs. 26%, p=0.001) and mother-reported SCAS (69% vs. 22%, p<0.001) but not for the father-reported SCAS (35% vs. 19%, p=0.156).

Of the seven studies reported on anxiety remission, 163, 198, 206, 237, 239, 242, 254-262 four defined remission as clinically significant change on the child-reported SCAS at the end of treatment, varying from 8 to 16 weeks from baseline. 163, 198, 206, 242 One study reported outcomes for three separate arms compared with wait-list: telephone, email, and client-initiated CBT.²⁰⁶ The pooled estimate of effect (averaging across multiple study arms in the study with more than 1 active arm) yielded an RR of 2.68 (**Appendix G Figure 18,** 95% CI, 1.48 to 4.88; N=321; k=4; I^2 =48%). Of these four studies, one also reported clinically significant change favoring CBT on the mother-reported SCAS (51.8% vs. 11.3%, p \leq 0.001) and father-reported SCAS (41.8 vs. 9.8, p≤0.001). Another reported clinically significant change favoring CBT on the mother-reported SCAS (26% vs. 6%, p=0.032) but not for the father-reported SCAS (4% vs. 7%, p=1.00). ²⁴² One of these four studies also reported no clinically significant change on a parent-reported SCAS (32.0% vs. 20.83%, p=0.38. 198 The fifth study defined remission as a LSAS-CA score of 30 or less and reported statistically significant differences favoring CBT (47% vs. 6%, p=0.0009).²³⁹ The sixth study defined remission as a ADIS-CSR score less than 4 and reported statistically significant differences favoring CBT (66.7% vs. 10.0%, p=0.011).²³⁷ The seventh study defined remission as a CGI-S score of 2 or less and a CGI-I score of 1.262 The study reported no statistically significant differences on the CGI-S (35.9% vs. 27.1%, p=0.49) or the CGI-I (20.4%) vs. 15.0%, p=0.61).

Nineteen studies reported on loss of anxiety diagnosis using a variety of measures (presence or absence of primary anxiety diagnosis or any anxiety diagnosis) using clinical interviews (ADIS, K-SADS, DISCAP, and Structured Clinical Interview for DSM-IV [SCID]). 163, 167, 177, 178, 183, 190, 195, 196, 198, 203, 206, 220, 224, 238, 241, 242, 244, 246, 251, 253-262, 275

Of the 19 studies, 17 reported on loss of any diagnosis, measured primarily using the ADIS structured clinical interview at the end of treatment (6 weeks to 6 months from baseline). $^{163, 167, 177, 183, 190, 195, 196, 198, 203, 206, 224, 238, 241, 242, 244, 246, 251, 253-262}$ Fifteen could be pooled. $^{163, 167, 177, 183, 190, 195, 196, 198, 224, 241, 242, 246, 251, 253}$ The pooled estimate of effect (averaging across multiple study arms in studies with more than one active arm $^{246, 251}$) yielded an RR of 3.09 (**Appendix G Figure 19**, 95% CI, 1.98 to 4.80; N=1,414; k=15; I^2 =65%). Of the remaining two studies, one study did not report sufficient data to permit pooling but reported statistically significant differences when comparing each of three CBT arms (telephone, email, or client initiated) with a wait-list control. 206 A second study also could not be pooled because the authors reported on a more expansive definition of loss of diagnosis (presence or absence of anxiety diagnosis or symptoms); 203 this study also reported statistically significant differences favoring the CBT arm.

Fourteen studies reported on loss of the primary anxiety diagnosis, measured primarily using the ADIS structured clinical interview, at the end of treatment with outcomes measured ranging from 6 weeks to 12 months from baseline. ^{163, 177, 178, 183, 190, 196, 198, 206, 220, 224, 242, 246, 251, 253, 275} Of these, 13 could be pooled. ^{163, 177, 178, 183, 190, 196, 198, 220, 224, 242, 246, 251, 253, 275} The pooled estimate of effect (averaging across multiple study arms in studies with more than one active arm ^{220, 246, 251, 275}) yielded an RR of 3.02 (**Appendix G Figure 20**, 95% CI, 1.84 to 4.95; N=1,079; k=13; *I*²=75%). One study did not report sufficient data to permit pooling but reported statistically significant differences across three CBT arms (telephone, email, or client initiated) when compared with a wait-list control. ²⁰⁶

Pharmacotherapy vs. Placebo

All pharmacotherapy studies reported on clinical response; all reported statistically significant improvement favoring pharmacotherapy; detailed outcomes are in **Appendix F Table 8**. Five (2 on fluoxetine, 2 on sertraline, and 1 on escitalopram) reported on clinician-rated response defined as moderately or markedly improved symptoms at the end of treatment, varying from 8 to 12 weeks from baseline (CGI-I scores of 1 or 2); ^{168, 169, 238, 244, 254-262} the pooled RR was 2.11 (95% CI, 1.58 to 2.98; N=370; k=5; I^2 =18%). Four of the five studies reported statistically significant differences favoring the intervention arms; the fifth study, focusing on selective mutism, did not report statistically significant differences in clinician- or teacher-rated CGI-I scores but did report statistically significant results for parent ratings on the CGI-I scale. ¹⁶⁹

A sixth study, on fluvoxamine, defined response as CGI-I less than 3; that is, the authors included minimal improvement (CGI-I=3) at 8 weeks as response. $^{225-228}$ The study reported statistically significant differences favoring fluvoxamine (76% vs. 29%, p<0.001) but did not report statistically significant differences with the more traditional definition of response (CGI-I <3). The seventh study, on duloxetine, defined response as 50 percent improvement on PARS severity for GAD. 243 The study reported statistically differences favoring duloxetine (59% vs. 42%, p \leq 0.05).

Three studies reported on remission at the end of treatment (9 to 12 weeks from baseline, **Table 10**); detailed outcomes are in **Appendix F Table 9**. These included two sertraline studies^{238, 254-262} and one duloxetine study.²⁴³ These results could not be pooled because the measurement of the outcome varied. The results were not consistent across the varied measures. One study limited the definition of remission to CGI-I=1, that is, marked improvement in symptoms, and reported no statistically significant differences at 9 weeks (18% vs. 0%, calculated p=0.28).²³⁸ A second study included CGI-I=1 as a definition of remission but also looked at CGI-S less than or equal to 2 and loss of diagnosis as additional measures of remission at 12 weeks and found that the only measure yielding statistically significant differences favoring the intervention arm was loss of diagnosis. The results favored the sertraline arm when compared with the placebo arm (45.9% vs. 23.7%; OR, 2.84 [95% CI, 1.01 to 4.67]; p=0.05).²⁶² A third study defined remission as CGI-S less than or equal to 2 or as PARS severity for GAD less than or equal to 8 at 10 weeks and reported results favoring duloxetine for both measures.

Combination Therapy (Sertraline Plus CBT) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. ²⁵⁴⁻²⁶² The study reported statistically significantly higher odds (OR, 13.6 [95% CI, 6.9 to 26.8]; p<0.001) of response (CGI-I of 1 or 2)²⁵⁴ and loss of diagnosis based on structured clinical interview (OR, 7.47 [95% CI, 2.63 to 12.64]; p=0.01)²⁶² at 12 weeks but not remission, defined as CGI-S score of 2 or less and CGI-I score of 1. For remission, the confidence intervals were very wide and spanned the null. ²⁶²

Results: All-Cause Mortality

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

No CBT studies reported on all-cause mortality.

Pharmacotherapy vs. Placebo

One study of duloxetine reported no deaths during the 10-week treatment in either arm.²⁴³ No other pharmacotherapy studies reported on all-cause mortality.

Combination Therapy (Sertraline Plus CBT) vs. Placebo

No studies of combination therapy reported on all-cause mortality.

Results: Quality of Life and Functioning

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

Twelve studies reported on functioning and quality-of-life outcomes after CBT treatment, when compared with wait-list, TAU, or placebo controls; detailed outcomes are in **Appendix F Table 10.** 163, 178, 183, 190, 196, 224, 242, 246, 251, 253-262, 275 Of these, eight studies, offering individual or group CBT to parents, children, or both, reported on CGAS scores at the end of treatment (with

outcomes measured ranging from 4 to 14 weeks). ^{178, 183, 190, 196, 224, 251, 253-262} With the exception of one study focusing on selective mutism, ¹⁷⁸ studies enrolled youth with GAD or any anxiety disorder. Three studies reported parent-reported CAIS scores. ^{246, 253, 255} The pooled estimate of effect for CGAS (**Table 11**) indicated statistically significant improvement for participants in the CBT arm when compared with participants in the control arm. For CAIS, however, inconsistencies in direction of effect across the studies resulted in differences between the arms that spanned the null.

Other measures of functioning such as the Child Anxiety Life Interference Scale (CALIS), Child Anxiety Life Interference Scale-Child (CALIS-C), Pediatric QOL Inventory-P, Quality of Life Inventory for Children [QOLI], PQ-LES-Q, and sleep-related problems were reported in one or two studies. 163, 242 Results were mixed or did not demonstrate statistically significant differences.

Pharmacotherapy vs. Placebo

Three studies (duloxetine, 243 fluoxetine, 168 and sertraline $^{254\text{-}262}$) reported on CGAS scores (a measure of functioning) at the end of treatment (10 to 12 weeks). **Table 11** presents pooled estimates of effect for CGAS showing statistically significant differences favoring the pharmacotherapy when compared with placebo. Two studies reported on functional remission (CGAS scores \geq 70). One, on duloxetine, reported a statistically significant difference between arms favoring duloxetine (59% vs, 42%, p \leq 0.05), and the other, on fluoxetine, reported no statistically significant difference.

The sertraline study also reported parent- and child-reported school functioning (CAIS)²⁵⁹ and sleep-related problems.²⁵⁸ Child-reported outcomes were not statistically significant. Some parent-reported outcomes (Child Anxiety Impact Scale-Parent) and sleep-related problems associated with separation (but not dysregulated sleep overall) were statistically significantly improved in the treatment arm when compared with placebo.

Combination Therapy (Sertraline Plus CBT) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. ²⁵⁴⁻²⁶² The study reported on multiple measures of symptoms including CGAS, ²⁵⁴ CAIS, ²⁵⁵ and sleep-related problems. ²⁵⁵ CGAS scores were significantly different at 12 weeks favoring combination therapy (calculated mean difference: 8.50 [95% CI, 5.55 to 11.45]²⁵⁴) as were parent-reported measures of CAIS at followup (7.4 vs. 15.2, adjusted p<0.001²⁵⁵) and sleep problems related to separation (p=.01), but not for child-reported measures of functioning (CAIS)²⁵⁹ or other sleep problems. ²⁵⁸

Results: Findings for Specific Populations

Appendix F Table 11 presents qualitative results for specific populations. No studies reported on results by gender identity or sexual orientation.

Subgroup Analyses

Four CBT studies reported analyses of specific populations. ^{167, 190, 241, 254, 262} All four studies reported analyses by age. ^{167, 190, 241, 255, 260} Two studies^{241, 255} reported no statistically significant differences in self-, ^{241, 255} parent-, ²⁵⁵ or clinician-reported²⁴¹ measures of symptomatology or severity by age. A third study reported significantly higher response rates at post-treatment, but not at 1-year follow-up, for older participants who received CBT when compared with TAU. ¹⁹⁰ A fourth study reported significantly higher rates of loss of diagnosis at post-treatment and 1-year follow-up for younger participants (7 to 10 years) receiving child and parent-focused CBT in comparison with those receiving child-focused CBT. ¹⁶⁷ Two studies reported analyses by sex. ^{167, 241} One²⁴¹ reported no statistically significant differences for clinician-rated severity or self-reported measures of anxiety by sex and the second ¹⁶⁷ reported significantly higher rates of loss of diagnosis at post-treatment and 1-year follow-up for female participants receiving child and parent-focused CBT. One study reported analyses by race and ethnicity. ^{256, 261} No statistically significantly more severe anxiety symptoms for participants of Hispanic ethnicity who received CBT. ²⁵⁶

Three pharmacotherapy (duloxetine, ²⁴³ fluvoxamine, ²²⁵⁻²²⁸ and sertraline ²⁵⁴⁻²⁶²) studies reported analyses for populations of interest. All three studies reported analyses by age. ^{226, 243, 255, 260} Three studies reported no statistically significant differences in symptoms, ²⁵⁵ symptom severity, ²⁴³ and all evaluated outcomes ²²⁶) by age. All three studies reported analyses by sex. ^{226, 243, 259} Two studies ^{226, 243} reported no statistically significant sifferences in for evaluated outcomes (GAD severity in one study ²⁴³ and all outcomes in the other study ²⁵⁶) by sex. One study ²⁵⁹ reported significantly less parent-reported, but not youth-reported, anxiety-related school impairments among males who received Sertraline compared to pill placebo. Two studies ^{226, 261} reported analyses by race. Both reported no statistically significant differences in anxiety symptomalogy or severity, ²²⁶ response ^{226, 261} or remission or loss of diagnosis ²⁶¹ by race. One study reported analyses by ethnicity. ²⁵⁶ Parents reported significantly more severe anxiety symptoms for participants of Hispanic ethnicity who received Sertraline.

One study²⁵⁴⁻²⁶² of combined pharmacotherapy and CBT reported analyses for symptoms,^{255, 256, 259} response and remission,²⁶¹ by age,^{255, 260} sex,²⁵⁹ ethnicity,²⁵⁶ or race.²⁶¹ No statistically significant differences in symptoms were reported by age.²⁵⁵ Statistically significant differences favored combined treatment in parent-reported psychosocial functioning were reported by sex.²⁵⁹ Parents, but not youth, reported a greater benefit in anxiety-related school impairments among males who received sertraline in combination with CBT than among females when compared with placebo recipients.²⁵⁹ No statistically significant differences in response, remission, or relapse were reported by race²⁶¹ or ethnicity.²⁵⁶

Findings Within Age Groups

Categorization of studies into groups mapping to children or adolescents is challenging. Three studies limited their inclusion to young children, with ages ranging from 3 to 7 years. ^{183, 195, 237} Four studies limited inclusion to adolescents only, with ages ranging from 13 to 20 years. ^{239, 242, 244, 253} The remaining 22 studies were focused on older children (5 to 14 years; 12 studies) ^{165, 167, 167}

^{177, 178, 196, 203, 206, 220, 240, 241, 251} or children and adolescents (7 to 18; 10 studies). ^{163, 168, 169, 190, 198, 224, 225, 238, 243, 254} Although studies varied in their specific inclusion criteria and whether they included adolescents, the majority of studies had a mean age between 10 and 14 years.

The results for young children only and adolescents only are largely consistent with the results for the entire evidence base in demonstrating benefit for symptom improvement.

For younger children, all three studies focused on CBT and reported consistent statistically significant benefits for anxiety symptoms in two^{183, 237} of three studies. ^{183, 195, 237} Two studies reported on response and both reported statistically significant differences favoring CBT. ^{195, 237} The single studies reporting on remission²³⁷ and functioning, ¹⁸³ respectively, suggested statistically significant differences favoring CBT. The results for loss of diagnosis were not consistently statistically significant in favoring CBT in the two studies reporting on this outcome. ^{183, 195}

For adolescents, three studies^{239, 242, 253} reported on CBT and one reported on pharmacotherapy, specifically escitalopram.²⁴⁴ Two^{239, 242} of the three^{239, 242, 253} CBT studies reported consistent statistically significant improvement in anxiety symptoms, response, and remission; one reported no statistically significant differences.²⁵³ Only one CBT study reported on loss of diagnosis and found no statistically significant differences.²⁵³ Two studies reported on functioning, and neither consistently found statistically significant differences.^{242, 253} The escitalopram study reported improvement in symptoms and response.²⁴⁴

Depression

Summary

We included 13 fair-quality RCTs for KQ 4¹⁷⁴⁻¹⁷⁶, ¹⁸⁵, ¹⁸⁷, ²⁰⁴, ²⁰⁷, ²¹⁶, ²³³, ²⁴⁸, ²⁴⁹, ²⁵², ²⁶⁶ (described in 20 publications ¹⁸⁶, ²⁰⁵, ²⁰⁸⁻²¹¹, ²¹⁷). Seven RCTs ¹⁷⁶, ¹⁸⁷, ²⁰⁴, ²⁰⁵, ²¹⁶, ²¹⁷, ²⁴⁸, ²⁴⁹, ²⁶⁶ were new in this update for KQ 4. One study that was included in the previous USPSTF report on depression treatment and screening for KQ 4 was excluded from this report for ineligible intervention. This study tested citalopram, which was not included in the current review. ²⁷⁷ Detailed study, population, intervention characteristics, and results are provided in **Appendix I Tables 25 through Table 30**. Detailed outcomes are provided in **Appendix F Table 14 through Table 28**. Meta-analysis forest plots are provided in **Appendix G Figure 25 through Figure 32**.

Study Characteristics

The characteristics of the included studies are summarized in **Table 12**. Six RCTs admitted children or adolescents meeting DSM criteria for MDD, ^{175, 176, 185, 207, 216, 252} and five RCTs admitted those with MDD based on a clinical interview (K-SADS, K-SADS-EC, MINI). ^{204, 233, 248, 249, 266} Two RCTs admitted children with MDD, dysthymia, or depressive disorder not otherwise specified and enrolled a sample in which more than 50 percent of participants met DSM criteria for MDD. ^{174, 187} Eight RCTs set a threshold for severity, ranging from requiring clinical important symptoms to specific minimum thresholds on BDI-II, CDRS-R, Hamilton Depression Rating Scale (HAM-D), and PHQ-9. ^{185, 187, 207, 216, 233, 248, 249, 252}

Mean ages ranged from 5 to 17.5 years. ^{204, 205, 249} One RCT focused on early childhood (ages 3 to 6 years); ^{204, 205} two focused on older children and adolescents (age ranges from 7 to 14 years and 6 to 17 years); ^{187, 252} and 10 focused on adolescents (age ranges from 12 to 17 years to 15 to 19 years). ^{174-176, 185, 207, 216, 233, 248, 249, 266} Two had a majority male participants. ^{187, 204, 205} Eight RCTs provided statistics on race, with the exception of one study with 71 percent Hispanic participants. ²¹⁶ White participants were a majority in all RCTs that reported race. ^{176, 185, 187, 204, 205, 207, 233, 252}

Common exclusion criteria were substance misuse or substance use disorder; bipolar disorder, schizophrenia, or other serious mental health disorders; intellectual disability; autism spectrum disorders; and suicide-related concerns.

Two pharmacotherapy RCTs investigated escitalopram. ^{185, 252} One three-arm trial compared included a group that received fluoxetine. ²⁰⁷ The most commonly assessed psychotherapy was CBT. Six RCTs focused on CBT. ^{174-176, 187, 248, 249} Among these, two included individual CBT, ^{175, 176} one family CBT, ¹⁸⁷ one group CBT, ¹⁷⁴ and two internet-delivered CBT. ^{248, 249} Three RCTs studied psychotherapies other than CBT. One focused on interpersonal psychotherapy ²¹⁶ and the other on Parent Child Interaction Therapy-Emotion Development. ^{204, 205} One RCT studied collaborative care. ²³³ One focused on internet-based psychodynamic therapy. ²⁶⁶

Eleven RCTs (2 on pharmacotherapy, 8 on psychotherapy, 1 on collaborative care) had a single active treatment compared with attention control or supportive contact, wait-list control, TAU, or placebo. Both pharmacotherapy RCTs compared escitalopram with placebo. ^{185, 252} Psychotherapy studies compared treatment with attention control, ^{248, 249} supportive contact, ²⁶⁶ wait-list control, ^{204, 205} TAU, ^{175, 176, 216} or placebo. ¹⁸⁷ The collaborative care study compared the intervention with enhanced usual care; treatments included a choice of antidepressants, brief CBT, or both. ²³³ Another trial, using a collaborative care approach, is discussed under psychotherapy because all participants in the active arm received CBT. ¹⁷⁵ One RCT had two active arms, group CBT with and without parent session, compared with wait-list control. ¹⁷⁴ One RCT had three active arms (fluoxetine, CBT, and fluoxetine plus CBT) compared with placebo. ²⁰⁷

Two pharmacotherapy trials compared escitalopram with placebo. ^{185, 252} One three-arm trial compared fluoxetine, CBT, and placebo. ²⁰⁷ One study compared collaborative care with enhanced usual care. ²³³ Six studies focused on CBT. ^{174-176, 187, 248, 249} Among these, two compared individual CBT with TAU, ^{175, 176} one compared family CBT with placebo, ¹⁸⁷ one compared group CBT with and without additional parent sessions with wait-list, ¹⁷⁴ and two compared internet-delivered CBT with an attention control group. ^{248, 249} Three studies focused on counseling other than CBT. ^{204, 216, 266} One compared interpersonal psychotherapy and TAU, ²¹⁶ the second compared Parent Child Interaction Therapy-Emotion Development with a wait-list control, ^{204, 205} and the third compared internet-based psychodynamic therapy with supportive contact. ²⁶⁶

Intervention durations ranged from 8 weeks to 12 months. Most studies reported results at the end of treatment. All 13 RCTs reported on continuous outcomes for depression symptoms. The most commonly reported measures were the CDRS-R^{176, 185, 187, 207, 233, 252} and BDI. ^{174, 216, 248, 249}

Nine RCTs reported response, ^{175, 176, 185, 207, 233, 248, 249, 252, 266} ten RCTs reported remission, ^{175, 176, 185, 187, 207, 216, 233, 248, 249, 266} and five RCTs reported loss of depression diagnosis. ^{174, 204, 205, 207, 248, 249} Three RCTs reported anxiety outcomes, ^{248, 249, 266} three studies reported suicide-related outcomes, ^{176, 185, 207, 252} and nine studies reported functioning outcomes. ^{174, 176, 185, 187, 204, 205, 207, 216, 233, 252} Five studies reported harms. ^{185, 207, 233, 252, 266} No psychotherapy studies reported harms.

RCTs relied on in-person delivery of interventions, except for two that reported on internet-delivered CBT^{248, 249} and one that reported on internet-based psychodynamic therapy.²⁶⁶

Half the RCTs advertised widely for recruitment; ^{174, 187, 207, 248, 249, 252, 266} three recruited from health systems and pediatric clinics; ^{175, 176, 233} one RCT recruited from preschools, daycares, primary care, and mental health facilities; ^{204, 205} one RCT recruited from mental health clinics; ²¹⁶ and one RCT did not specify the recruitment setting. ¹⁸⁵ Ten studies were conducted in the United States, ^{174-176, 185, 187, 204, 205, 207, 216, 233, 252} and three studies were conducted in Sweden. ^{248, 249, 266}

Results: Depression Symptoms

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

Ten studies reported outcomes related to changes in depression symptoms. ¹⁷⁴⁻¹⁷⁶, ¹⁸⁷, ²⁰⁴, ²⁰⁷, ²¹⁶, ²⁴⁸, ²⁴⁹, ²⁶⁶ All outcomes for each study are reported in **Appendix I**, and for outcomes reported by at least three studies, we conducted meta-analyses (**Appendix G**). **Table 13** presents pooled estimates of the effect for end-of-treatment measures, specifically the BDI/BDI-II, ¹⁷⁴, ²¹⁶, ²⁴⁸, ²⁴⁹ CDRS-R, ¹⁷⁶, ¹⁸⁷, ²⁰⁷ and HAM-D¹⁷⁴, ¹⁷⁵, ²¹⁶ scales. Two of the pooled effects (BDI/BDI-II and HAM-D) suggested a statistically significant benefit of treatment compared with controls, while the third pooled estimate (CDRS-R) demonstrated no significant effect.

Several studies also reported other measures of depression symptoms in addition to measures that we pooled (Appendix F Table 14). For some studies, findings from these additional measures (Mood and Feelings Questionnaire, 249 mean CGI-I and CGI-S, 216 and Revised Children's Anxiety and Depression Scale [RADS]²⁰⁷) were consistent with what has already been reported by those studies using BDI, BDI-II, CDRS-R, or HAM-D measures. In other cases, findings were not consistent. Two studies by the same author of the same intervention (individual, in-person CBT) compared with TAU, which included any health services, including psychopharmacotherapy, provided by their usual care provider, reported using the CES-D and found mixed results. ^{175, 176} One of these studies, published in 2005, reported larger, but nonstatistically significant different improvements in CES-D scores at 52 weeks, consistent with findings from the HAM-D outcomes also reported in that study. ¹⁷⁵ The later of the two studies, published in 2016, larger, statistically significant improvements in CES-D scores at 52 weeks, consistent with reported benefits for the CDRS measure at 52 weeks. ¹⁷⁶ These larger improvements in the treatment group persisted at 104 weeks but were no longer statistically significant, also consistent with CDRS findings at 104 weeks. ¹⁷⁶ A third study reported a larger improvement in PHQ-9 score for the treatment group, but this difference was not statistically significant.²⁴⁸ A fourth study evaluated parent-child interaction therapy focused on emotion development compared with wait-list controls and reported outcomes at 18 weeks using the K-SADS-CD MDD core score and the Preschool Feelings Checklist scale.²⁰⁴ Participants allocated

to the treatment had statistically significant larger improvements on both outcomes (p<0.000). ²⁰⁴ Lastly, a study comparing internet-based psychodynamic therapy with supportive contact found no statistically significant difference in the primary outcome measured by the Quick Inventory of Depressive Symptomatology for Adolescents (QIDS-A17-SR); a secondary outcome of Montgomery Åsberg Depression Rating Scale—self-rated (MADRS-S) demonstrated a difference favoring the active treatment. ²⁶⁶

Pharmacotherapy vs. Placebo

Three studies reported on the effects of pharmacotherapy on depression symptoms when compared with placebo (2 on escitalopram^{185, 252} and 1 on fluoxetine²⁰⁷) (**Appendix F Table 15**). Three studies reported on outcomes at the end of treatment using CDRS-R, ^{185, 207, 252} two reported the CGI-I and CGI-S, ^{185, 252} and one reported RADS. ²⁰⁷ Study sample sizes ranged from 109²⁰⁷ to 158. ¹⁸⁵

Table 13 reports pooled differences on the CDRS-R indicating statistically significant benefit favoring pharmacotherapy. Results on other measures did not always yield statistically significant differences favoring pharmacotherapy. On the CGI-S, Emslie et al¹⁸⁵ reported a significant difference favoring escitalopram when compared with placebo at 8 weeks, whereas Wagner et al²⁵² did not report a statistically significant difference. March et al²⁰⁷ did not find a statistically significant difference between fluoxetine and placebo on the RADS at 12 weeks.

Combination Therapy (Fluoxetine Plus CBT) vs. Placebo

One study comparing fluoxetine plus CBT to placebo reported on depression symptoms measured by the CDSR-R and RADS-2 (**Appendix F Table 16**).²⁰⁷ The results were consistent for CDSR-R and RADS-2 in reporting statistically significant benefits for fluoxetine plus CBT. There was a statistically significant difference in the change in CDSR-R from baseline to 12 weeks when compared with placebo (33.79 vs. 41.8, p=0.001). There was also a statistically significant difference in the change in RADS-2 from baseline to 12 weeks when compared with placebo (56.95 vs. 66.7, p=0.001).

Collaborative Care vs. Treatment as Usual

One study comparing a collaborative care intervention with TAU reported on depression symptoms measured by the CDSR-R (**Appendix F Table 17**). Intervention patients had an 8.5-point greater decrease in mean CDRS-R score from baseline than treatment-as-usual participants (95% CI, -13.4 to -3.6; p=0.001) at 6 months and a 9.4-point greater decrease from baseline at 12 months (95% CI, -15.0 to -3.8; p=0.001). A test of the interaction between group effects and time was statistically significant at p<0.001.²³³

Results: Response, Remission, or Loss of Diagnosis

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

Regarding response, three studies reported responses on the BDI and BDI-II scale (**Appendix F Table 18**). ^{216, 248, 249} These studies could not be pooled because of the varied thresholds used; however, all reported statistically significant differences favoring psychotherapy.

Other measures of response included $CGI \ge 2^{207,\,210}$ and $<5^{176}$ depression symptoms for 8 weeks and fulfilling the Reliable Change Index $^{266,\,278}$ The results were not consistent. One study defined response as CGI greater than or equal to 2 and did not report statistically significant differences. $^{207,\,210}$ Another study defined response defined as 8 or more weeks below with the threshold of five or more depression symptoms necessary for full diagnosis but where full recovery has not yet occurred; the results were statistically significantly different favoring CBT at 52 and 104 weeks from baseline. 176 A third study used the Reliable Change Index, that is, a way to ensure that the magnitude of change for individuals is statistically reliable, while scoring 2 standard deviations below the pretreatment mean and found a statistically significant difference favoring the active treatment. 266

Two studies defined remission as a CDRS-R score \leq 28; neither reported statistically significant differences. ^{187, 207, 210} A third study defined remission as a QIDS-A17-SR score of 6 or lower and found a statistically significant difference favoring the active treatment. ²⁶⁶

One study reported on recovery, defined as longer than or equal to 8 weeks of no or minimal symptoms on weekly Diagnostic Status Ratings ($\leq 1-2$) and little or no impairment. The results were statistically significantly different favoring CBT at 52 and 104 weeks from baseline. ¹⁷⁶

Five studies reported on loss of diagnosis. ^{174, 204, 207, 210, 248, 249} Of these, four (all in adolescents) reported sufficient data to be pooled. ^{174, 207, 248, 249} The pooled estimate and results from individual studies favored the treatment arms, but the confidence intervals spanned the null. A fifth study, ²⁰⁴ of parent-child interaction therapy in young children (mean age: 5 years), could not pooled with the other studies but also reported results favoring the psychotherapy arm. Specifically, the study reported adjusted odds ratios when comparing the control arm with the intervention of 9.52 (95% CI, 8.44 to 10.74). ²⁰⁴

Pharmacotherapy vs. Placebo

One study on escitalopram and one on fluoxetine reported response defined as the proportion of participants with CGI-I \leq 2. Neither study found statistically significant differences between pharmacotherapy and placebo (**Appendix F Table 19**).

All three pharmacotherapy studies (2 on escitalopram and 1 on fluoxetine) reported on the proportion of participants with CDRS-R score less than or equal to 28 at the end of treatment (8 or 12 weeks). This measure was termed as remission in two studies ^{185, 207, 210} and response in one. ²⁵² **Table 14** presents pooled results. The pooled estimate and results from individual studies favored treatment arms, but the confidence intervals spanned the null. ^{185, 207, 210, 252}

One study on fluoxetine reported loss of MDD diagnosis based on K-SADS-P/L interview and found that a significantly greater proportion of those receiving fluoxetine no longer met MDD criteria at 12 weeks compared with placebo (78.6% vs. 60.4%, p=0.007). 207, 210

Combination Therapy (Fluoxetine Plus CBT) vs. Placebo

One study^{207, 210} found that the combination therapy arm had a higher and statistically significant rate of response (CGI-I \leq 2: 71.0% vs. 34.8%; p=0.0001²⁰⁷), remission (CDRS-R \leq 28: 37% vs. 17%; OR: 3.0 [95% CI, 1.58 to 5.79]²¹⁰), and loss of diagnosis (no longer meeting DSM-IV criteria for MDD using the K-SADS-P/L: 85.3% vs. 60.4%; OR: 4.1 [95% CI, 2.00 to 8.44]²¹⁰) when compared with placebo (**Appendix F Table 20**).

Collaborative Care vs. Treatment as Usual

The collaborative care study found intervention participants were more likely than treatment-as-usual patients to achieve depression response (\geq 50% reduction in CDRS-R score from baseline) by 12 months (OR, 3.3 [95% CI, 1.4 to 8.2]; p=0.009) but not by 6 months (OR, 3.1 [95% CI, 1.2 to 7.9]; p=0.02). Intervention participants were significantly more likely to achieve depression remission (PHQ-9 < 5) at both 6 months (OR, 5.2 [95% CI, 1.6 to 17.3]; p=0.007) and 12 months (OR, 3.9 [95% CI, 1.5 to 10.6]; p=0.007) (**Appendix F Table 21 and Table 22**). ²³³

Results: All-Cause Mortality

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

No studies reported on all-cause mortality.

Pharmacotherapy vs. Placebo

No studies reported on all-cause mortality.

Combination Therapy (Fluoxetine Plus CBT) vs. Placebo

No studies reported on all-cause mortality.

Collaborative Care vs. Treatment as Usual

No studies reported on all-cause mortality.

Results: Functioning

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

Six studies reported functioning outcomes, including quality-of-life outcomes. ^{174-176, 204, 205, 207, 211, 216} Four Four Four on CGAS could be pooled; the results

suggested no statistically significant differences (**Table 15**). A fifth study,²⁰⁴ of parent-child interaction therapy in young children, did not report exact p-values and could not pooled with the other studies, but the results favor psychotherapy with a Cohen's d of 1.16, p<0.0001.

In addition to CGAS, studies also reported functioning with other measures (Appendix F Table 23). Nearly all studies reported larger improvements in functioning or quality of life with treatment; however, most studies were not powered on these outcomes; thus, estimates may have been imprecise and may not have reached statistical significance. One study reported functioning using the SAS-SR and reported statistically significant larger improvements with interpersonal psychotherapy compared with TAU (school-based clinic care), ²¹⁶ and a second reported significantly larger improvements in functioning as measured by the PECFAS²⁰⁴ and total sleep problems as measured by CBCL;²⁰⁵ these findings were consistent with CGAS outcomes also reported by these studies. A third study reported no statistically significant differences in functioning at 12 weeks between participants allocated to individual, in-person CBT compared with no CBT with a placebo pill as measured with the HoNOSCA and PQ-LES-Q measures, also consistent with CGAS findings of no effect for this study. ^{207, 211} In a fourth study, despite finding a statistically significant favorable effect of individual, in-person CBT compared with TAU at 52 weeks as measured by CGAS, the authors observed differences in quality of life as measured by the PEDS-QL measure that were not statistically significant. ¹⁷⁶ A fifth study reported statistically significant improvements in the mental health component score of the Short-Form 12 (SF-12) for an individual, in-person CBT compared with TAU; SF-12 physical component scores and the CGAS scores were also improved more with treatment, but these results were not statistically significant. ¹⁷⁵ Finally, a sixth study reported statistically significant larger improvements in functioning as measured by the Global Assessment of Functioning for the two variations of group CBT intervention compared with placebo. 174

Pharmacotherapy vs. Placebo

Three studies reported functioning outcomes, including quality of life (**Appendix F Table 25**). ^{185, 207, 252} Pooled results for CGAS indicated statistically significant differences favoring pharmacotherapy (**Table 15**).

In addition to change in CGAS scores, one study reported outcomes using the HoNOSCA and PQ-LES-Q measures. Although participants allocated to treatment showed larger improvements on these measures consistent with CGAS outcomes, findings were not statistically significant. In addition, the proportion of participants achieving a CGAS score of less than 70 (the threshold associated with no impairment) was 20 percent in the treatment group compared with 19 percent in the placebo group (p=NS).

Combination Therapy (Fluoxetine Plus CBT) vs. Placebo

The Treatment for Adolescents with Depression Study (TADS) study reported functioning outcomes.^{207, 211} In this study, combination therapy was associated with larger improvement in functioning as measured by the CGAS, HoNOSCA, and PQ-LES-Q at 12 weeks compared with no CBT/placebo control (**Appendix F Table 27**).

Collaborative Care vs. Treatment as Usual

The collaborative care study measured functional status on the Columbia Impairment Scale. Differences between the intervention and control arms were not significant at an a priori p-value threshold of less than or equal to 0.01 at 6 months (mean difference, -4.4 [95% CI, -8.4 to -0.5]; p=0.03) or 12 months (mean difference, -4.3 [95% CI, -8.3 to -0.3]; p=0.04).²³³

Results: Findings for Specific Populations

Subgroup Analyses

Appendix F Table 29 presents qualitative results for specific populations. Two CBT studies reported analyses for specific populations. ^{174, 207-211} One study reported analyses by age. ²⁰⁸ Adolescents who were younger than 16-years-old at baseline had significantly greater improvement in clinician-rated symptom severity than adolescents who were 16 or older across all treatment conditions. ²⁰⁸ No statistically significant differences in functioning were reported by age. ²¹¹ Two studies reported no statistically significant differences in functioning ²¹¹ or recovery rates ¹⁷⁴ by sex. One study reported no statistically significant differences in functioning by race or ethnicity. ²¹¹

Two pharmacotherapy studies (escitalopram²⁵² and fluoxetine²⁰⁷⁻²¹¹) reported analyses for specific populations. Both studies reported on functioning outcomes by age. ^{211, 252} One study reported that 12- to 17-year-old adolescents, but not 6- to 11-year-old children, in the treatment group had significantly better improvements on a clinician-rated measure of functioning than their counterparts in the pill placebo group. ²⁵² One study reported no statistically significant differences in clinician- or self-reported functioning by age. ²¹¹ Both studies reported on symptom severity by age. ^{208, 252} One study reported that 12- to 17-year-old adolescents, but not 6- to 11year-old children, in the treatment group had significantly better improvements on measures of symptom severity than their counterparts in the pill placebo group. ²⁵² One study reported that adolescents who were younger than 16-years-old at baseline had significantly greater improvement in clinician-rated symptom severity than adolescents who were 16 or older across all treatment conditions. ²⁰⁸ One study reported on symptom improvement by age. ²⁵² The study found that 12- to 17-year-old adolescents, but not 6- to 11-year-old children, in the treatment group had significantly better clinician-rated improvement in symptoms than their counterparts in the pill placebo group. One study reported no statistically significant differences in functioning by sex, race, or ethnicity.²¹¹

One study²⁰⁷⁻²¹¹ of combined pharmacotherapy (fluoxetine) and CBT reported analyses on symptom severity²⁰⁸ and overall functioning²¹¹ by age,²⁰⁸ sex,²¹¹ or race/ethnicity.²¹¹ Adolescents who were younger than 16-years-old at baseline had significantly greater improvement in clinician-rated symptom severity than adolescents who were 16 or older across all treatment conditions.²⁰⁸ No statistically significant differences in functioning were reported by age, sex, or race/ethnicity.²¹¹

Findings Within Age Groups

One study of psychotherapy (parent-child interaction therapy) restricted inclusion to young children, ages 3 to 6 years, with a mean age of 5 years.²⁰⁴ The study reported statistically significant benefit for symptoms, loss of diagnosis, and functioning for psychotherapy. We found no studies of pharmacotherapy in children.

Two studies recruited both children and adolescents. One study on omega-3, individual-family psychoeducational psychotherapy, and their combination recruited children from ages 7 to 14 years, with a mean age of 11.6 years. ¹⁸⁷ The study found that individual-family psychoeducational psychotherapy when compared with placebo did not produce statistically significant differences for symptoms or remission. A second study, on escitalopram, recruited children from 6 to 17 years, with a mean age of 12.3 years. The study found no statistically significant differences for symptoms, response, or functioning. ²⁵²

All other studies were restricted to adolescents only, with ages for inclusion ranging from 12 to 19 years and mean age ranging from 14.6 to 17.5 years. One study had three arms contributing to evidence on psychotherapy, pharmacotherapy, and their combination. In all, the evidence on adolescents included seven studies on psychotherapy, ^{174-176, 207, 216, 248, 249} two on pharmacotherapy, ^{185, 207} one on combination therapy, ²⁰⁷ and one on collaborative care, ²³³ and their results are described in the main results above.

Anxiety or Depression

We included two studies of fair quality (described in 3 articles) that studied children with anxiety or depression. ^{184, 263, 264} Detailed study, population, intervention characteristics, and results are provided in **Appendix I Tables 35 through Table 40**.

Study Characteristics

One study (N=51) included participants ages 12 to 17 years (mean age: 15.8) with a primary diagnosis of any DSM-IV anxiety disorder (including obsessive compulsive disorder) or depression. The second study (N=185) included children and adolescents ages 8 to 16 years (mean age: 11.3) meeting DSM-IV criteria for full or probable diagnoses of separation anxiety, GAD, social anxiety disorder, MDD, dysthymic disorder, or minor depression. In both studies, anxiety disorders were more common than depressive disorders. Female participants constituted 57 percent to 58 percent of the samples. The majority of participants were Hispanic (59%, excluding non-Hispanic White participants) in one study and White in the other (excluding Hispanic participants).

Both studies offered a transdiagnostic approach drawing on cognitive science, with a minimum of eight weekly sessions. One study offered up to maximum of 12 sessions. ¹⁸⁴ and the other up to 21 sessions. ^{263, 264} The comparison group was put on a wait-list in one study. or offered an assisted referral in the other. ^{263, 264}

The studies reported on anxiety and depression symptoms and functioning. Additionally, one study reported on response at 16 weeks (end of treatment)²⁶³ and response and remission at 32 weeks ²⁶⁴

Both studies were conducted in the United States and included clinical referrals and self-referrals. The results below describe outcomes for the overall sample in each study.

Results: Anxiety Symptoms

Psychotherapy Interventions vs. Wait-List or Assisted Referral Controls

One study (mean age: 15.8 years) reported ADIS clinician severity rating scale and reported statistically significant differences favoring treatment at followup (4.1 vs. 5.4 at 8 weeks, p<0.006) and change from baseline to followup. The threshold for meeting the criteria for diagnosis is 4. The second study (mean age: 11.3 years) reported on PARS and similarly found statistically significant improvements at followup (16 weeks) and change from baseline to followup; the study reported followup values of PARS below 12 (the threshold for clinical response 279) in both arms (8.6 vs. 11.4). 263, 264 The benefits continued to be statistically significantly different at 32 weeks (p=0.003, details not reported). 264

Both studies reported on CGI-S and CGI-I scores. Both reported statistically significant differences for CGI-S favoring treatment (2.6 vs. 3.4, calculated mean difference -0.80 [95% CI, -1.19 to -0.41]; ¹⁸⁴ 4.1 vs. 5.1, mean difference: -1.00, p<0.006²⁶³) and CGI-I (2.3 vs. 3.1, calculated mean difference -0.80 [95% CI, -1.23 to -0.37]; ¹⁸⁴ 3.04 vs. 4.00, mean difference: -0.96, p=0.016²⁶³) favoring transdiagnostic treatment over wait-list or assisted referral.

Results: Depression Symptoms

Psychotherapy Interventions vs. Wait-List or Assisted Referral Controls

One study reported results for RCADS scores at the end of treatment and the second on CDRS-R scores at the end of treatment at 16 weeks and at 32 weeks. Neither study reported statistically significant differences for measures of depression. However, as noted above, both studies reported significantly different CGI-S and CGI-S scores at followup, favoring transdiagnostic treatment over wait-list or assisted referral.

Results: Response, Remission, and Loss of Diagnosis

Psychotherapy Interventions vs. Wait-List or Assisted Referral Controls

One study reported statistically significant results favoring treatment for response, defined as CGI-I \leq 2, posttreatment at 16 weeks (56.8% vs. 28.2%, p<0.001)²⁶³ and at 32 weeks (67.5% vs 4.31%²⁶⁴). The differences for remission (36.3% vs. 22.2%) at 32 weeks, defined as CGI-I=1, favored transdiagnostic treatment over assisted referral but were not statistically significant (p=0.06).²⁶⁴

Results: All-Cause Mortality

No studies reported on all-cause mortality.

Results: Quality of Life and Functioning

One study reported no statistically significant differences in the Adolescent Life Interference Scale (ALIS) at 8 weeks. ¹⁸⁴ The second study reported statistically significant differences favoring treatment in CGAS at 16 (68.5 vs. 61.9, p= 0.001^{263}) and 32 weeks (70.9 vs. 65.0, p= 0.004^{264}); CGAS scores greater than or equal to 70 represent functional remission.

Results: Findings for Specific Populations

Subgroup Analyses

One study reported that ethnicity moderated response to transdiagnostic treatment, with Hispanic youths having a heightened response and greater improvements in functioning than other participants when compared with Hispanic youths in the assisted referral arm.²⁶³

Findings Within Age Groups

One study¹⁸⁴ included adolescents only with recruitment restricted to ages 12 to 17 years and a mean age of 15.8 years, and a second study^{263, 264} included both children and adolescents with inclusion ranging from 8 to 16 years and a mean age of 11.3 years. Neither reported results for children versus adolescents.

KQ 5. What Are the Harms of Treatment (Psychotherapy, Pharmacotherapy, or Collaborative Care) in Children and Adolescents Who Are Treated for Depression, Anxiety, or Suicide Risk?

Suicide Risk

Summary

We included two RCTs of good or fair quality (described in 4 articles). ^{179-181, 192} Detailed study, population, and intervention characteristics are provided in **Appendix I Table 16**.

Study Characteristics

The characteristics of the included studies are summarized in **Table 4**. Two studies admitted children based on elevated suicide risk. ^{179-181, 192}

Mean ages ranged from 14 to 16 years. Included studies focused on adolescence: one study included adolescents 11 to 17 years ¹⁷⁹⁻¹⁸¹ and one study included adolescents 12 to 18 years. ¹⁹² The majority of both samples were female. ^{179-181, 192} One study included mostly White Scottish adolescents, ¹⁹² and one study did not report race or ethnicity. ¹⁷⁹⁻¹⁸¹

Included studies examined family therapy¹⁷⁹⁻¹⁸¹ and MBT.¹⁹² Both studies compared intervention with TAU. Duration of treatment ranged between six and 12 sessions over 12 months. No evidence was captured that examined pharmacotherapies.

The two included studies^{179-181, 192} reported on any adverse events, and one study¹⁷⁹⁻¹⁸¹ reported on incidence of serious adverse events and other harms. Time of measurement across outcomes ranged from 12 weeks to 4 years.

The two included studies recruited participants from child and adolescent mental health services in the United Kingdom. ^{179-181, 192} One study ¹⁷⁹⁻¹⁸¹ was rated good quality, and one study ¹⁹² was rated fair quality.

Results: Other Adverse Events

One study¹⁷⁹⁻¹⁸¹ reported on adverse events, serious adverse events, and other harms during the 12- to 18-month followup period. Similar numbers of adverse events, including attendance at minor injury units, walk-in centers, accident and emergency centers, and re-referral to mental health services, occurred in the family therapy group (54%) and treatment-as-usual group (52%). Serious adverse events, defined as hospital attendance, also occurred at similar rates across the intervention (38%) and control (34%) arms. Two participants assigned to the family therapy group died between 3 and 4 years post-randomization. Neither death was related to self-harm. One additional study¹⁹² reported five adverse events among four participants, but the occurrences were not considered to be trial related and not reported by group.

Results: Findings for Specific Populations

Subgroup Analyses

No study reported on harms for specific populations.

Findings Within Age Groups

Both studies were in adolescents only.

Anxiety

Summary

As noted previously, we limited the synthesis to CBT for psychotherapy; we included pharmacotherapies approved by the FDA for children and adolescents. Eleven studies of good or

fair quality addressed harms (described in 22 articles). 168, 169, 224-228, 238, 239, 242-244, 253-262 Detailed study, population, intervention characteristics, and results are provided in **Appendix I Table 24**.

Study Characteristics

Four studies evaluating CBT, ^{224, 239, 242, 253} six evaluating pharmacotherapy, ^{168, 169, 238, 243, 244} and one study with three arms evaluating CBT, sertraline, and combination therapy ²⁵⁴⁻²⁶² addressed harms. **Table 16** describes these studies in detail.

Results: Suicide Deaths, Suicide Attempts and Deliberate Self-Harm, or Suicidal Ideation

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

Two studies of individual CBT reported on suicidal ideation, attempts, or self-harm behavior. ²⁵³⁻²⁶² One study (internet, child plus parent) of 60 participants ²⁵³ reported that two participants in the wait-list control group withdrew from the study because of risk of suicide by 17 weeks; the study did not note similar withdrawals in the CBT arm. A second child-focused in-person study reported on self-harm behavior without suicidal attempt (1/139 [0.7%] vs. 0/76 [0%]), suicidal ideation (5/139 [3.6%] vs. 1/76 [1.3%]), and suicidal attempts (no events in either arm) by 12 weeks. ²⁵⁴⁻²⁶²

Pharmacotherapy vs. Placebo

Three studies reported on suicide-related harms at the end of treatment at 8 to 12 weeks (duloxetine, ²⁴³ escitalopram, ²⁴⁴ and sertraline ²⁵⁴⁻²⁶²). No studies reported suicide deaths, two studies reported on suicide attempts (1/26 for escitalopram vs. 0/25 events for placeb; ²⁴⁴ no events in 1 study for either sertraline or placebo ²⁵⁴⁻²⁶²); three reported on suicidal ideation or worsening of suicidality (1/135 vs. 0/137 for duloxetine vs. placebo; ²⁴³ 6/26 for escitalopram vs. 2/25 for placebo; ²⁴⁴ 0/133 for sertraline vs. 1/76 for placebo ²⁵⁴⁻²⁶²), and two studies reported on self-injurious behavior (2/26 for escitalopram vs. 1/25 for placebo; ²⁴⁴ 1/133 for sertraline vs. 0/76 for placebo ²⁵⁴⁻²⁶²) (**Appendix F Table 12**). Suicide-related harms were rare, and the differences were not statistically significantly different.

Combination Therapy (Pharmacotherapy and Psychotherapy) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. ²⁵⁴⁻²⁶² The study reported more self-harm behaviors without suicide attempts (1.4% [2/140] vs. 0) and suicidal ideation (3.6% [5/140] vs. 1.3% [1/76]) in the combination arm at 12 weeks, but no suicide attempts in either arm. ²⁵⁴

Results: Other Adverse Events

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

Two child-focused studies of individual CBT reported on serious adverse events. ²⁵⁴⁻²⁶² One study of 73 participants ^{239,} reported a single adverse event in the wait-list control group of

hospitalization due to the need to remove a dental brace by 31 weeks. No serious adverse events were reported in either arm in the other study by 12 weeks. 254-262

Four studies reported on withdrawal due to side effects for treatments ranging from 10 to 14 weeks. $^{224, 242, 253-262}$ The studies varied in type of CBT: they included individual and group therapy, delivered in person and on the internet, and child-focused and child and parent therapy. The RR of withdrawal due to side effects was 0.39 (95% CI, 0.08 to 1.87; N=372; k=5; I^2 =0%, **Appendix G Figure 33**).

One study reported no homicidal ideation or events in either arm of an individual in-person child-focused CBT when compared with placebo by 12 weeks. 254-262

Pharmacotherapy vs. Placebo

Three studies reported on serious adverse events (duloxetine, ²⁴³ escitalopram, ²⁴⁴ and sertraline ²⁵⁴⁻ ²⁶²). The escitalopram study reported one individual experiencing serious adverse events in both arms. ²⁴⁴ The other two studies reported one individual experiencing serious adverse events in the treatment arm and none in the placebo arm. ^{243, 254}

Five studies (1 each on duloxetine, ²⁴³ escitalopram, ²⁴⁴ fluvoxamine, ²²⁵⁻²²⁸ and sertraline, ²⁵⁴⁻²⁶² and fluoxetine ¹⁶⁸) reported on withdrawal due to adverse events. Together, the RR of withdrawal across all drugs was 1.72 (95% CI, 0.57 to 5.18; N=734; k=5; *I*²: 26%; **Appendix G Figure 34**). The risk of withdrawal due to adverse events appeared to be elevated for fluvoxamine and fluoxetine.

One study reported that two participants (1.5%) experienced homicidal ideation (but no homicidal attempts in the intervention and none in placebo arm).²⁵⁴

Fluoxetine studies reported greater frequency¹⁶⁸ or severity¹⁶⁹ of some adverse events. adverse events reported at statistically higher frequency in the pharmacotherapy arm included gastrointestinal events^{168, 225} and neurological complaints.¹⁶⁸ Although other pharmacotherapy studies reported higher frequency of some other harms in the treatment arm when compared with placebo, the differences did not reach statistical significance at p=0.05 (**Appendix F Table 13**).

Combination Therapy (Pharmacotherapy and Psychotherapy) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. ²⁵⁴⁻²⁶² The study reported few or no occurrences of serious adverse events (1 event in the combined therapy arm and no events in the placebo arm), withdrawal due to adverse events (1 event in each arm), homicidal ideation (no events in either arm), and homicidal attempts (no events in either arm). The study did, however, report a higher frequency pf psychiatric adverse events (29.3% vs. 13.2%, calculated absolute risk difference: 16/100 [95% CI, 5 to 27]) and all harms-related adverse events, that is, self-injurious behavior and homicidal ideation (10.0% vs. 1.3%, calculated absolute risk difference: 9/100 [95% CI, 3 to 14]) in the combined therapy arm when compared with placebo.

Results: Findings for Specific Populations

Subgroup Analyses

One study with three arms (CBT, sertraline, and CBT plus sertraline)^{167, 190, 241, 254-262} reported on harms for specific populations. The authors reported that the rate of psychiatric adverse events, but not physical adverse events, was significantly higher in children compared to adolescents across all treatment arms.²⁶⁰ The rate of overall adverse events was significantly higher in children than adolescents who received sertraline.²⁶⁰

Findings Within Age Groups

No studies reported on harms in young children.

Results for older children or children and adolescents are described above.

Results for studies of adolescents only suggested lower rates of harms for CBT^{239, 242, 253} and higher rates of harms for escitalopram, ²⁴⁴ but results were not statistically significant.

Depression

Summary

We included seven studies for KQ 5 (described in 12 articles). ^{173, 176, 185, 186, 207-211, 233, 252, 266} All KQ 5 studies are also included in KQ 4 except for one meta-analysis, which was new to this review update. ¹⁷³ One study that was included in the previous USPSTF report on depression was excluded from this report for ineligible intervention. This study tested citalopram, which was not included in this current update. ²⁷⁷

Study Characteristics

The characteristics of the included studies are summarized in **Table 17**. Detailed study, population, intervention characteristics, and results are provided in **Appendix I Table 32 through Table 34**. Detailed outcomes are provided in **Appendix F Table 30 through Table 38**.

Results: Suicide Deaths, Suicide Attempts and Deliberate Self-Harm, or Suicidal Ideation

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

Two studies of CBT interventions reported on suicide-related events (**Appendix F Table 30 and Table 31**). Table 30 Suicide-related events included suicide attempts and new or worsened ideation. Both reported higher but not statistically significantly different rates in the treatment arm. One study, comparing CBT plus TAU with TAU, reported five events among 106 participants (4.7%) in the CBT with TAU arm compared with two events among 106 participants (1.9%) in the TAU arm (RR, 2.50 [95% CI, 0.50 to 12.60]). At study entry, all had recently declined or discontinued antidepressants prematurely. During a year-long followup, a minority of

participants received antidepressants in each arm (9.4% in the CBT plus TAU arm and 7.6% in the TAU arm). The second study, TADS, ^{207, 209} reported inconsistent results across various TADS publications. TADS included four study arms: CBT, fluoxetine, combined CBT and fluoxetine, and a placebo comparator. The events reported by parents and patients were reviewed and subsequently recoded using the Columbia-Classification Algorithm for Suicidal Assessment in a reanalysis. The first analysis published by study authors in 2004 reported five events among 109 participants (4.6%) in the CBT arm compared with four events among 112 participants (3.6%) in the placebo arm (RR, 1.26 [95% CI, 0.35 to 4.57]). ²⁰⁷ Safety results of reanalyzed data published in 2006 reported three (2.7%) events in the placebo arm, resulting in a higher RR of 1.68 (95% CI, 0.41 to 6.87).²⁰⁹ An extended analysis of TADS was published in 2009 that included suicide-related events through blinded (baseline to week 12) and unblinded phases (week 12 to week 36) of the trial. ²⁸⁰ These analyses are not eligible for the current systematic review because they include events that occurred after unblinding and clinical management of nonresponders. However, the publication included a graphic indicating that five suicide-related events occurred in the placebo arm by week 12, of which two occurred in participants on SSRIs at the time of the event. The placebo arm did not appear to include TAU: the authors reported that they discarded a community-based TAU group because of concerns about variability and access to care. 207 No further details or per-protocol analyses are available from the authors. A per-protocol analysis that reassigns placebo participants receiving SSRIs to the pharmacotherapy arm would change the denominators and, therefore, relative risks for all comparisons in the study.

The TADS study reported no statistically significant differences on suicidal ideation measured by the SIQ-Jr scale.²⁰⁷

Pharmacotherapy vs. Placebo

Three studies reported on suicide-related outcomes using a variety of measures (**Appendix F Table 32 and Table 33**). One study explicitly reported that no completed suicides occurred; the others did not report data on deaths. ^{207, 209, 252} The two escitalopram studies reported similar rates of events potentially related to suicide or self-harm when compared with placebo (1 event among 129 participants [0.8%] vs. 2 events among 132 participants [1.5%]; ²⁵² 6 events among 157 participants [3.8%] vs. 6 events among 155 participants [3.9%] ¹⁸⁵). The fluoxetine study (TADS)^{207, 209} reported inconsistent results across various publications on suicide-related events. The first analysis published by study authors in 2004 suggested a higher but nonstatistically significant rate of suicide-related events in the fluoxetine arm when compared with placebo (9 events among 109 participants [8.3%] vs. 4 events among 112 participants [3.4%]; RR, 2.31 [95% CI, 0.73 to 7.29]). ²⁰⁷ Safety results published in 2006 reported 10 (9.2%) events in the intervention and three (2.7%) in the placebo arm resulting in a higher RR, 3.43 (95% CI, 0.97 to 12.11). ²⁰⁹

Two studies reported no statistically significant differences on suicidal ideation measured by the SIO-Jr scale. 185, 207

One network meta-analysis examined harms across a range of drugs and populations, including those ineligible for the current review (**Appendix I Table 34**). The rate of suicide-related

behaviors or ideation events appeared similar for escitalopram versus placebo (15/290 [5%] vs. 15/294 [5%], 2 studies) and for fluoxetine versus placebo (51/521 [10%] vs. 44/514 [9%], 7 studies). 173

Pharmacotherapy Plus CBT vs. Placebo

A single study on combination therapy, the TADS trial, reported on suicide-related events, with results varying by publication source (**Appendix F Table 34 and Table 35**). The first analysis published by study authors in 2004 reported six suicide-related events among 107 participants (5.6%) in the combined arm compared with four events among 112 participants (3.4%) in the placebo arm (RR, 1.57 [95% CI, 0.46 to 5.41]). Safety results published in 2006 reported five (4.7%) events in the intervention and three (2.7%) in the placebo arm, resulting in a higher RR, 1.75 (95% CI, 0.43 to 7.12).

One study reported a statistically significant difference on suicidal ideation measured by the SIQ-Jr scale, favoring combination therapy (mean score at followup: 11.79 vs. 15.01, p=0.02) in adjusted analyses but not in comparisons of mean differences.²⁰⁷

Collaborative Care vs. Treatment as Usual

The study did not report suicide-related outcomes.

Results: Other Adverse Events

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

No study reported on withdrawal due to adverse events. The TADS study reported no differences in rate of harm-related adverse events (which included self-harm without suicidal intent, suicide attempt, and harm to others) in the CBT arm when compared with placebo (5 events among 111 participants [4.5%] vs. 6 events among 112 participants [5.4%, OR: 0.8 [95% CI, 0.25 to 2.81]) (**Appendix F Table 36**). One study used an open-ended question on the QIDS-A17-SR to assess potential negative effects and found that no participant in the treatment arm deteriorated reliably on the QIDS-A17-SR when compared with three participants in the control arm.

Pharmacotherapy vs. Placebo

Two escitalopram trials reported on withdrawal due to adverse events and serious adverse events (**Appendix F Table 37**). One trial reported higher rates in the treatment arm for both outcomes (4 (2.6%) withdrawals in the treatment arm and 1 (0.6%) in the placebo arm; 4 (2.6%) serious adverse events in the treatment arm and 2 (1.3%) in the placebo arm¹⁸⁵). The second reported similar rates in both arms for both outcomes (2 [1.5%] withdrawals due to adverse events vs. 2 [1.5%]; 2/131 [1.5%] serious adverse events vs. 3/133 [2.3%]).²⁵² These differences were not statistically significantly different in either study.

The fluoxetine study (TADS) study reported a higher but not statistically significantly different rate of harm-related adverse events in the combined therapy arm when compared with placebo

(13 events among 109 participants [11.9%] vs. 6 events among 112 participants [5.4%, OR: 2.4, [95% CI, 0.87 to 6.54]).²⁰⁷

Pharmacotherapy + CBT vs. Placebo

No study reported on withdrawal due to adverse events. The TADS study reported a higher but not statistically significantly different rate of harm-related adverse events in the combined therapy arm when compared with placebo (9 events among 107 participants [8.4%] vs. 6 events among 112 participants [5.4%, OR: 1.6 [95% CI, 0.56 to 4.72]) (**Appendix F Table 38**). 207

Collaborative Care vs. Treatment as Usual

A single trial of collaborative care found no differences in psychiatric hospitalizations among intervention patients compared with control patients (6% vs. 4%, respectively). More control patients experienced an ED visit with a primary psychiatric diagnosis than intervention patients (1 [2%] vs. 5 [10%] patients, respectively); however, this study was not powered to detect differences.²³³

Results: Findings for Specific Populations

Subgroup Analyses

No study reported on harms for specific populations.

Findings Within Age Groups

The only study in children did not report on harms.²⁰⁴

One of the two studies in children and adolescents, specifically on omega-3, individual-family psychoeducational psychotherapy, and their combination, did not report on the harms of individual-family psychoeducational psychotherapy when compared with placebo. ¹⁸⁷ One study on escitalopram reported similar or lower rates of harms in the treatment arm. ²⁵²

The remainder of the studies reported on adolescents only; the results are summarized above.

Anxiety or Depression

Results: Suicide Deaths, Suicide Attempts and Deliberate Self-Harm, or Suicidal Ideation

No studies reported on suicide outcomes.

Results: Other Adverse Events

No studies reported on other adverse events.

Results: Findings for Specific Populations

No study reported on harms for specific populations.

Chapter 4. Discussion

Summary of Evidence

We summarize the evidence, including strength of evidence ratings, by KQ in **Table 18**.

Benefits of Screening (Key Question 1)

We did not identify any studies reporting on the direct benefits of screening.

Screening Test Accuracy (Key Question 2)

We only identified one study assessing the accuracy of screening for suicide risk in adolescents evaluated against a clinical diagnostic interview reference standard; the instrument used was the SRS, a 20-item instrument that was embedded in a longer questionnaire, and the study population was recruited from youth identified as potential high school dropouts.²⁴⁷ We rated the strength of evidence for screening as insufficient because of inconsistency in estimates based on the reference standard used, imprecision, and study limitations. Given that most depression screening instruments include an assessment of suicidal ideation, it is unclear whether a separate, stand-alone instrument to screen for increased suicide risk has value for universal screening in primary care practice. The Ask Suicide Screening Questions (ASQ) is a brief 4-item instrument that was initially developed for youth age 8 years or older in emergency department settings but has since been evaluated in other medical settings including outpatient specialty and primary care. 281, 282 The Joint Commission recommends suicide risk screening for all medical patients in all medical settings, including outpatient practices. ²⁸³ The National Institute for Mental Health developed an ASQ toolkit to support implementation of suicide risk screening in medical settings, including for youth in primary care.²⁸⁴ We identified one study evaluating the ASQ in outpatient settings, including primary care, but we excluded it because its accuracy was compared against another suicide risk screening instrument and not against a diagnostic clinical interview by a qualified professional.²⁸²

We identified evidence for test accuracy related to seven different instruments for screening for MDD, but five of those instruments were limited to single-study bodies of evidence. ^{172, 199, 219, 223} Across this body of evidence, the sensitivity of screening tests compared with clinical diagnostic interview ranged from 0.59 to 0.94, and we rated most comparisons as low strength of evidence. Specificity ranged from 0.53 to 0.97, and we rated this body of evidence as moderate strength of evidence. All but one study were focused exclusively on adolescents.

The depression module (PHQ-9) of the full PHQ is the instrument highlighted for use in screening for depression by the AAP in a quality improvement collaborative designed to improve diagnostic performance for depression. ²⁸⁵ The Centers for Medicare & Medicaid Services Meritbased Incentive Payment System and the National Committee on Quality Assurance HEDIS measure set include a depression screening quality measure that is applicable to persons age 12

and older. ²⁸⁶⁻²⁸⁸ These measures require that standardized screening tools normalized and validated based on age for which they are being used should be used for screening, but they do not specify a specific tool. Similarly, the AAP Guidelines for Adolescent Depression in Primary Care recommended screening using a formal self-report tool. ¹⁴⁷ For these measures and guidelines, multiple tools are listed, but the CES-D is the only instrument included in this review update that are among the listed examples. We identified one study of the accuracy of the full PHQ modified for adolescents, and we identified no studies evaluating the PHQ-9, which is the depression module of the full PHQ. The PHQ-9 may offer advantages over the CES-D with respect to feasibility of implementation because it is already the basis for quality measures related to monitoring depression remission and response to treatment and includes an item specific to suicidal ideation (unlike the CES-D). However, the full PHQ, which also includes modules for anxiety, somatoform disorders, eating disorders, and substance abuse, may be more feasible for use as a transdiagnostic screener compared to the use of separate screeners for different conditions. ²⁸⁹

Based on the accuracy characteristics for the one included study of PHQ-A in this update review, ¹⁹⁹ per 1,000 screening tests conducted, 58 false-positives and eight false-negatives would be generated at the low end of MDD prevalence (3%), and 53 false-positives and 30 false-negatives would be generated at the high end of prevalence (11%). As noted above, we did not identify any evidence related to the harms of screening. The relative frequency of false-negatives is smaller than the number of false-positives, and most of the other instruments included in this update follow a similar pattern. Positive results would require additional diagnostic evaluation to sort out true-positives from false-positives, but it is likely that some youth screening positive but not meeting diagnostic criteria for MDD may have PDD (formerly known as dysthymia) or other behavioral health conditions with symptoms similar to depression. The consequences of a false-negative would largely depend on the severity of the missed diagnosis; the likelihood of missing a severely depressed youth is small because most screen-detected depression is likely to be mild to moderate. However, even mildly to moderately depressed youth may have suicidal ideation, and the consequences of missing such symptoms could be serious.

We examined nine different instruments (i.e., ANS, PHQ-A, PI-ED, SAS, SASA, SCARED, SPAI, SPIN, and SWQ) to screen for anxiety, most of which screened for specific anxiety disorders such as GAD, social anxiety disorder, separation anxiety disorder, and panic disorder. Some screening instruments with subscales screened for more than one anxiety disorder. Thus, we evaluated 15 different approaches (e.g., full scale, subscales) for detecting anxiety disorders, and we had only a single study body of evidence for nine of the approaches (from four studies). Across all of the screeners and subscales and thresholds for a positive test evaluated, sensitivity ranged between 0.34 and 1.00; we rated most comparisons low strength of evidence. Specificity for this body of evidence ranged between 0.47 and 0.98, and we rated about half of the comparisons as moderate strength of evidence and the other half as low strength of evidence. The confidence intervals around the estimates of sensitivity and specificity were often wide, indicating a lack of precision for most screeners. Of the 10 studies that assessed screeners to detect anxiety, four included both children and adolescents, and the remainder included adolescents only.

In all but two studies, youth were the respondents, and in one of the two both youth and parents completed the same screeners.¹⁷¹ This study administered both the full and the short versions of the SCARED to parents and youth ages 9 to 13 years. Sensitivity was greater for the screeners in which youth were the respondents, suggesting that youth are better reporters of their own distress. However, there were more false-positives per 1,000 screens for the youth-administered screeners. Specificity was only minimally worse when youth were the respondents.

One screener designed to detect panic disorder, the ANS, is notable for the perfect sensitivity in all three versions—two items, three items, and five items. The perfect sensitivity of the ANS does not appear to be related to the fact that adolescents were respondents because most of the other screeners were given to youth, and the ANS is the only one with such high sensitivity. In fact, the PHQ-A, which also included adolescents as respondents, had a much lower sensitivity when compared with a clinical diagnosis of panic disorder. Rather, it is more likely that the targeted nature of the ANS's content contributed to its ability to perfectly detect adolescents with panic disorder. The two gateway items concerned sudden physical and mental feelings of fright or anxiety. In contrast, the PHQ-A is a broader tool used more often to detect depression as well as other mental health disorders.

The difference in accuracy between a broad screening tool and one that is more targeted is seen when comparing the SCARED full scale and some of the SCARED subscales. Sensitivity of the full-scale SCARED with youth as respondents was 0.76,¹⁷¹ whereas sensitivity on the SCARED separation anxiety scale was 0.88.²¹⁸ In contrast, the sensitivity of the more global SCARED GAD scale was 0.64.¹⁷¹

To facilitate adoption of screening in primary care, screeners should not only be accurate but be short. Both the SCARED and the SPIN have shorter versions that were administered in some of the included studies. The 10-item SCARED short version for youth was somewhat lower (0.67) than the full 41-item version (0.76) with respect to global anxiety symptoms. ¹⁷¹ With a sensitivity of 0.86, the 3-item Mini-SPIN²³² was equivalent to that of the 17-item SPIN (0.82)²³¹ Thus, accuracy was not compromised for the Mini-SPIN with respect to identifying social anxiety disorder.

Across all screeners and subscales, the rate of false-positives was as high as 500 per 1,000 screens for a range of prevalence values from 2.5 percent to 13 percent. In contrast, the rate of false-negatives for the same range of prevalence values did not exceed 100 per 1,000 screens. The consequences of a high rate of false-positives indicate that many families may needlessly be concerned about their children's mental health. However, good practice dictates that those who are screened positive should receive a clinical evaluation that can rule out an anxiety disorder. The consequences of the lower rate of false-negatives indicate that fewer truly anxious youth will be missed by a screening program. Yet, astute parents and primary care providers may recognize that even in the absence of screen-detected anxiety youth whose physical complaints include stomachaches, headaches, fatigue, or muscle tension without an organic cause may be manifesting anxiety. Good practice indicates that these youth may also benefit from a clinical evaluation for anxiety disorders.

Harms of Screening (Key Question 3)

We did not identify any studies reporting on the direct harms of screening for anxiety or depression. Two RCTs reported no increased distress or suicidal ideation following screening for suicide risk. ^{267, 268}

Benefits and Harms of Treatment (Key Questions 4 and 5)

Suicide

Sixteen RCTs of interventions to reduce suicide risk or self-harm addressed the benefits of treatment, $^{164, 179-182, 191-194, 197, 200-202, 212-215, 221, 222, 229, 236, 245, 265}$ and two reported on harms of treatment. $^{179, 192}$ Nine of 16 RCTs were new to this update. $^{164, 179-181, 192, 194, 202, 212-215, 221, 222, 229, 236}$ The previous review found statistically nonsignificant increases in suicide attempts for psychotherapy interventions and no benefits for suicidal ideation, raising the possibility of harm. ^{179, 192} One newly identified update to a previously included study found no statistically significant differences in suicide deaths but found benefits in all-cause mortality over the long term.²⁰¹ Newly identified studies do not report on suicide attempts, and the evidence base on self-harm events is inconsistent. The updated evidence base (including prior and new studies) suggests improvements in suicidal ideation resulting from treatment, but this finding was only statistically significant for one measure. The evidence suggested no statistically significant differences on all other outcomes. Notably, all studies included TAU comparators, which for ethical reasons must be active comparators, such as standard psychotherapy, individual counseling, family sessions, medication assessment and review, medication, and other care coordination activities. Comparable intensity of therapy in study arms, coupled with low event rates for some outcomes (such as suicide deaths, hospitalizations, and suicide attempts), is likely to make differences between study arms difficult to detect. We rated the evidence as low for benefit on suicidal ideation but insufficient for evaluating outcomes such as suicide attempts, hospitalizations, and deaths. Only two studies reported on various harms outcomes (such as attendance at minor injury units, walk-in centers, and accident and emergency centers; re-referral to mental health service; and hospital attendance). The available evidence did not indicate a higher frequency of events in the treatment arm. We rated the strength of evidence as low for no harm. Only one study reported analyses of specific populations. The evidence suggested that hospital attendance for self-harm events did not vary by age across adolescents.

Anxiety

Twenty-nine RCTs on treatment of anxiety in children and adolescents addressed benefits, ^{163, 165, 167-169, 177, 178, 183, 190, 195, 196, 198, 203, 206, 220, 224-228, 237-244, 246, 251, 253-262} and 11 addressed harms. ^{168, 169, 224, 238, 239, 242-244, 253-262} All are new in this update. These studies provided evidence on CBT, pharmacotherapy, and a combination of CBT and sertraline. Consistent, precise, statistically significant differences existed for most anxiety outcomes for CBT and pharmacotherapy, and we rated the strength as evidence as moderate for benefit for nearly all outcomes. For response, remission, loss of diagnosis, and functioning, the evidence suggests statistically significant

differences favoring CBT; there is less evidence for pharmacotherapy on these outcomes, but the available evidence indicates benefits for clinical response. Results were less consistent for other outcomes. The evidence on CBT is more voluminous (23 RCTs) compared with pharmacotherapy (7 RCTs). Most pharmacotherapy studies (6 of 7) required specific anxiety diagnoses, that is, GAD, separation anxiety, or social anxiety disorders, whereas a minority of CBT studies specified diagnosis (10 of 24). The remainder targeted any anxiety diagnosis. Anxiety studies covered a wide range of ages, from preschool (ages 3 to 7 years) ^{183, 195, 237} through adolescence, though 11 studies were focused exclusively on adolescents. Studies focusing on younger children (ages 3 to 7 years^{183, 195, 237}) were consistent with the overall findings in demonstrating benefits for symptoms and clinical response.

Few CBT trials reported on harm outcomes, and we rated the strength of this evidence as insufficient. The evidence suggests that suicide-related harms, serious adverse events, and withdrawal due to adverse events are rare in pharmacotherapy studies but more frequent in the treatment arm; thus, we rated this evidence as low for harms.

Few studies reported analyses by age, sex, race, or ethnicity. Studies reporting on analyses of anxiety symptoms consistently reported no effect of age or sex, but there is insufficient evidence available on anxiety symptoms by race or ethnicity. There is insufficient evidence available on specific populations for other outcomes.

Depression

Thirteen RCTs on treatment of depression in children and adolescents addressed benefits, ^{174-176, 185, 187, 204, 205, 207, 216, 233, 248, 249, 252} and five addressed harms. ^{176, 185, 207, 233, 252, 266} Eight RCTs were new in this update for KQ 4, all focusing on psychotherapy. ^{175, 176, 187, 204, 205, 216, 248, 249, 266} Additionally, one meta-analysis of pharmacotherapy is new to the update on harms. ¹⁷³ The prior report on depression in children and adolescents included two trials on psychotherapy; neither ^{174, 207} showed improvement on remission or recovery. These two trials were inconsistent on symptoms, response, and functioning. The updated evidence on psychotherapy suggests some benefits for symptom improvement, clinical response, and loss of diagnosis, but the results are not consistent across all measures for other outcomes. The evidence for pharmacotherapy suggests benefit for symptom improvement, but the results are not consistent across all measures for other outcomes. Thus, we rated the strength of evidence for psychotherapy and pharmacotherapy as low for benefit.

The evidence on harms is limited but suggests a higher frequency of suicide-related outcomes for psychotherapy and pharmacotherapy. Notably, one multi-arm trial (Treatment for Adolescent Depression Study, or TADS) with inconsistent reporting on suicide-related events across its various publications contributed to the evidence on psychotherapy, pharmacotherapy, and their combination. These discrepancies increase the uncertainty regarding harms of treatment and have led to a call for independent reanalysis of the TADS results. ^{290, 291} The FDA notes a higher frequency of suicide-related events in boxed warnings for antidepressants. ²⁹² The underlying FDA review for this warning relied on drug trials in populations ineligible for this review. ²⁹³

The prior report found very limited evidence on treatments in children: no psychotherapy trials and just one pharmacotherapy trial²⁵² recruited children younger than age 12 years. This updated review included two new studies in children. Of these, one recruited children ages 7 to 14 years, with an average age of 11.6.¹⁸⁷ This trial is a comparison of psychoeducation psychotherapy plus placebo vs. placebo, where the primary purpose was to examine the effectiveness of omega-3 fatty acids. The sample size for therapy and placebo arms together was 37 participants. The second study of children was a larger trial (N=229)^{204, 205} of parent-child interaction therapy (PCIT). The results were not consistent across the two studies: the PCIT trial suggested improved symptoms, loss of diagnosis, and improved functioning, whereas the psychoeducation psychotherapy did not find benefits for treatment for symptoms or remission.

Few studies reported analyses by age, sex, race, or ethnicity. The available evidence on functioning outcomes by age is inconsistent, and there is insufficient evidence available on functioning outcomes by sex, race, or ethnicity. There is insufficient evidence available for specific populations on other outcomes.

Limitations of the Evidence

We did not identify any direct evidence for the benefits of screening for suicide risk, anxiety, and depression and very limited evidence on harms for suicide risk alone, among children or adolescents in primary care or primary care—relevant settings. Despite the large number of potential instruments that could be used for screening, we identified only one to two studies for any given instrument for the KQ on test accuracy (KQ 2). Further, these studies often evaluated multiple thresholds for determining a positive test, but it is not clear whether the optimal thresholds reported by such studies would remain optimal when used across different age groups or populations. Existing quality measures related to depression screening list examples of several instruments that can be used, but we identified surprisingly little research for those tools. Although studies reporting psychometric characteristics of these tools exists, few have studies evaluating them against a reference standard that includes a clinical diagnostic interview. The PHQ-A is capable of screening across conditions (suicide risk, anxiety, depression), but it is only applicable to adolescents. Although other instruments are available that assess a broad range of mental, behavioral, and emotional health areas, such instruments are typically designed for epidemiologic studies or to augment clinical history-taking and diagnosis and are too long to be considered feasible for use as brief screening instruments in primary care settings. We identified no studies reporting on the harms of screening.

Related to the benefits and harms of treatment, fewer studies were conducted in children compared with adolescents. Although studies generally reported outcomes using validated measures of symptoms, minimally important differences in children and adolescents for these measures are lacking and whether statistically significant differences in mean symptoms scores are clinically meaningful is uncertain. Despite this limitation in such measures, response, remission, and loss of diagnosis outcomes generally mirrored changes in symptom scores, suggesting that the differences observed are likely clinically meaningful. For all conditions, heterogeneity in type and duration of psychotherapy interventions, underlying anxiety and

depression subtypes, risk factors, and comorbidities somewhat limited our certainty about the magnitude of benefit for such interventions.

For suicide studies, more than half the studies included participants with comorbid conditions but did not always report how these conditions were treated. Ongoing therapy for these comorbid conditions may have attenuated the effect of the interventions.

Trauma and maltreatment are risk factors for suicide, anxiety, and depression in children, ^{294, 295} but no trauma-focused interventions were found to be eligible for this review. Another constraint in interpreting the evidence for psychotherapy relates to the comparators. For suicide, the comparator arms generally included active comparators that may result in understated benefits for the intervention arm. For depression and anxiety, multi-arm studies of drugs, psychotherapy, and their combination,(TADS²⁰⁷⁻²¹¹ Child/Adolescent Anxiety Multimodal Study, or CAMS²⁵⁴⁻²⁶²) compared these active treatments with placebo. In these cases, the lack of blinding for the psychotherapy and combination therapy arms may also bias outcome reporting.

For pharmacotherapy interventions, the evidence is largely limited to short-term benefits (typically up to 12 weeks). The evidence for increased suicidal events across all three topics is hampered by imprecision because of rare events, conflicting reporting in the published studies for depression in particular, and varying definitions for this type of harm. The ethical considerations and logistical challenges of conducting studies in children often limit the size of trials; future research studies that employ the same type of study designs are likely to encounter similar difficulties with adequately powering trials for rare outcomes.

Treatment studies necessarily exclude low-risk participants from trials to maximize the potential for finding an effect. Screen-detected populations may include low-risk individuals; as a result, whether the benefit observed in treatment studies applies to screen-detected populations is unclear. Further, rates of treatment enrollment and retention in research studies are likely different than what can be expected in routine clinical practice.

Future Research Needs

More RCTs are needed on the benefits and harms directly arising from screening for suicide risk, anxiety, and depression among children and adolescents in primary care settings (or similar settings), when compared with no screening or usual care. Future research could also elucidate the advantages and disadvantages of combined screening for depression and suicide risk, as currently happens with some instruments (e.g., PHQ-9). Although some studies have demonstrated that screening for depression alone may not be adequate to identify those at high risk for suicide, such studies were conducted among hospitalized medically ill youth and may not be applicable to youth seen in primary care practice. ^{296, 297} Because multiple types of anxiety disorders exist, future research could elucidate trade-offs between screening instruments designed to identify any anxiety disorder versus instruments designed for specific anxiety disorders. Lastly, the use of computerized adaptive screening could be explored to allow for the use of broader screening instruments to screen across condition but yet limit respondent burden.

The existing evidence focuses on adolescents, reflecting the higher prevalence of mental health disorders among them. More research on treatment in children is also warranted, across all types of therapies. However, traditional RCTs randomizing individual treatments will necessarily be constrained in size (because of the challenges of recruitment in younger children and because of lower rates of depression and suicide risk) and, therefore, statistical power by ethical and logistical considerations. Cluster-randomized trials and pragmatic trials²⁹⁸ may help address size considerations for trials of children or adolescents but may also continue to carry risks of bias in outcome measurement because blinding is not likely to be feasible. Publication of hitherto unreported data on rare or no suicide events from ongoing and completed trials will help supplement the relatively sparse evidence on this outcome.

Studies infrequently measure long-term outcomes or conduct analyses of populations of interest. No studies reported on sexual orientation or gender identity in subgroup analyses; given that these are known risk factors for suicide in particular, further research is needed. In light of rising suicide rates among Black children, more work needs to be done on accurate identification and effective prevention of suicide risk among them. ¹¹⁰ No studies focused on American Indian youth, who have the highest rates of suicide deaths in the United States.

Little is known about minimal clinically important differences for the multitude of outcome measures evaluated in this report. Studies establishing these thresholds will help stakeholders interpret the existing evidence.

Limitations of the Review

We limited this review to studies published in English that were conducted in very highly developed countries to maximize applicability of findings to primary care settings in the United States. As a result of the restriction of the screening benefits (KQ 1) and accuracy (KQ 2) questions to primary care and primary care—relevant settings, this review does not address the outcomes from schoolwide or communitywide screening that may result in increased referrals to primary care.

Similarly, we limited the scope of the KQ on test accuracy (KQ 2) to screening instruments feasible for use in primary care settings. For suicide risk, this review was limited to evaluating the diagnostic accuracy of instruments to identify youth at high risk for suicide as compared with a diagnostic clinical interview and did not include predictive accuracy studies. Future reviews on this topic might consider including studies that evaluate the accuracy of screening instruments to predict future suicidal behavior (e.g., suicide attempts, nonfatal self-injury).

For our review, for suicide risk intervention and anxiety treatment questions, all participants in eligible trials needed to have an anxiety diagnosis or recognized suicide risk. As a result, we may have excluded studies with participants with subsyndromal anxiety or studies that included a spectrum of recognized suicide risk. We expanded the inclusion criteria for treatment studies of depression to those where 50 percent or more of participants had MDD in an attempt to identify studies that included other relevant depression diagnoses. Nonetheless, this criterion resulted in

the review excluding studies that may have otherwise been eligible and demonstrated benefit.^{299,} 300

Because questions on the treatment of these conditions are framed relatively narrowly to support a screening recommendation, eligible studies compared treatment with no treatment, usual care, or placebo. As a result, the review cannot speak to the suggested sequence of treatments (e.g., psychotherapy vs. pharmacotherapy for depression). Because ethical concerns limit the ability to conduct comparative studies for suicide prevention using placebo or wait-list controls, we included treatment-as-usual comparators with durations and intensity comparable to active arms. Nonetheless, this review does not summarize the state of evidence for studies comparing two active interventions simultaneously³⁰¹ or comparing usual care and active treatments sequentially,³⁰² as may be the case in some suicide prevention studies.

We limited the scope of pharmacotherapy agents to drugs approved by the FDA for pediatric use and often likely to be first-line therapy for treatment for screen-detected conditions because of their relevance to primary care. We also limited the scope of psychotherapy for anxiety to CBT; Appendix A summarizes the evidence for other available therapies. We refer readers to recent AHRQ Effective Health Care Program reviews for more comprehensive information about additional medications that may not be used as first-line treatment and comparative effectiveness of various psychotherapy and pharmacotherapy treatments for depression ¹⁵³ and anxiety ¹²³ in children and adolescents.

We also focused on health outcomes as benefits. Studies that focus on healthcare utilization (e.g., demonstrating an increase in referral or uptake of services) or intermediate outcomes would have been excluded from the review if they did not also report on health outcomes. In practice, achieving positive results following the implementation of an intervention requires adequate diagnostic followup (Appendix A, CQ 1) and engagement with care (Appendix A, CQ 6).

Conclusions

We found no eligible studies that reported on benefits directly arising from screening when compared with usual care or no screening. Limited direct evidence suggests no short-term harms from screening for suicide risk. The evidence for screening for suicide risk, anxiety, and depression in children and adolescents relies on indirect evidence on the accuracy of screening and the benefits and harms of treatment. Both pharmacotherapy and psychotherapy treatments have some benefit for some depression and anxiety outcomes (specifically, CBT for anxiety alone was reviewed); the evidence is limited for suicide risk interventions. Harms are rare in treatment studies but more frequent in pharmacotherapy arms when compared with placebo. Evidence gaps persist in children younger than age 11 years for test accuracy, depression and suicide risk interventions, and for screening and treatment differences by sex, race/ethnicity, sexual orientation, and gender identity.

References

- 1. Siu AL, U. S. Preventive Services Task Force. Screening for depression in children and adolescents: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med.* 2016 Mar 1;164(5):360-6. doi: 10.7326/M15-2957. PMID: 26858097.
- 2. Crosby AE, Ortega L, Melanson C. Self-directed violence surveillance: uniform definitions and recommended data elements. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2011.
- 3. Ivey-Stephenson AZ, Demissie Z, Crosby AE, et al. Suicidal ideation and behaviors among high school students—Youth Risk Behavior Survey, United States, 2019. *MMWR Suppl.* 2020 Aug 21;69(1):47-55. doi: 10.15585/mmwr.su6901a6. PMID: 32817610.
- 4. National Institute of Mental Health. Suicide. Bethesda, MD: National Institute of Mental Health; 2019. https://www.nimh.nih.gov/health/statistics/suicide.shtml. Accessed March 3, 2020.
- 5. Andover MS, Morris BW, Wren A, et al. The co-occurrence of non-suicidal self-injury and attempted suicide among adolescents: distinguishing risk factors and psychosocial correlates. *Child Adolesc Psychiatry Ment Health*. 2012 Mar 30;6:11. doi: 10.1186/1753-2000-6-11. PMID: 22463065.
- 6. Grandclerc S, De Labrouhe D, Spodenkiewicz M, et al. Relations between nonsuicidal self-injury and suicidal behavior in adolescence: a systematic review. *PLoS One*. 2016;11(4):e0153760. doi: 10.1371/journal.pone.0153760. PMID: 27089157.
- 7. Sellers CM, Diaz-Valdes A, Porter AC, et al. Nonsuicidal self-injury, suicide planning, and suicide attempts among high-risk adolescents prior to psychiatric hospitalization. *Res Child Adolesc Psychopathol*. 2021 Nov;49(11):1503-11. doi: 10.1007/s10802-021-00830-z. PMID: 34059987.
- 8. Robinson K, Garisch JA, Wilson MS. Nonsuicidal self-injury thoughts and behavioural characteristics: Associations with suicidal thoughts and behaviours among community adolescents. *J Affect Disord*. 2021 Mar 1;282:1247-54. doi: 10.1016/j.jad.2020.12.201. PMID: 33601703.
- 9. Voss C, Hoyer J, Venz J, et al. Non-suicidal self-injury and its co-occurrence with suicidal behavior: An epidemiological-study among adolescents and young adults. *Acta Psychiatr Scand*. 2020 Dec;142(6):496-508. doi: 10.1111/acps.13237. PMID: 32979220.
- 10. Jacobson CM, Gould M. The epidemiology and phenomenology of non-suicidal self-injurious behavior among adolescents: a critical review of the literature. *Arch Suicide Res.* 2007;11(2):129-47. doi: 10.1080/13811110701247602. PMID: 17453692.
- 11. Cha CB, Franz PJ, E MG, et al. Annual research review: Suicide among youth epidemiology, (potential) etiology, and treatment. *J Child Psychol Psychiatry*. 2018 Apr;59(4):460-82. doi: 10.1111/jcpp.12831. PMID: 29090457.
- 12. Hawton K, Harriss L. Deliberate self-harm in young people: characteristics and subsequent mortality in a 20-year cohort of patients presenting to hospital. *J Clin Psychiatry*. 2007 Oct;68(10):1574-83. PMID: 17960975.
- 13. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5), fifth edition. Arlington, VA: American Psychiatric Association; 2013.

- 14. Ferdinand RF, de Nijs PF, van Lier P, et al. Latent class analysis of anxiety and depressive symptoms in referred adolescents. *J Affect Disord*. 2005 Nov;88(3):299-306. doi: 10.1016/j.jad.2005.08.004. PMID: 16182373.
- 15. Foley DL, Goldston DB, Costello EJ, et al. Proximal psychiatric risk factors for suicidality in youth: the Great Smoky Mountains Study. *Arch Gen Psychiatry*. 2006 Sep;63(9):1017-24. doi: 10.1001/archpsyc.63.9.1017. PMID: 16953004.
- 16. Merikangas KR, Calkins ME, Burstein M, et al. Comorbidity of physical and mental disorders in the neurodevelopmental genomics cohort study. *Pediatrics*. 2015 Apr;135(4):e927-38. doi: 10.1542/peds.2014-1444. PMID: 25755242.
- 17. Melvin GA, Dudley AL, Gordon MS, et al. What happens to depressed adolescents? A follow-up study into early adulthood. *J Affect Disord*. 2013 2013/10/01/;151(1):298-305. doi: https://doi.org/10.1016/j.jad.2013.06.012.
- 18. Woodward LJ, Fergusson DM. Life course outcomes of young people with anxiety disorders in adolescence. *J Am Acad Child Adolesc Psychiatry*. 2001 Sep;40(9):1086-93. doi: 10.1097/00004583-200109000-00018. PMID: 11556633.
- 19. Leone M, Kuja-Halkola R, Leval A, et al. Association of youth depression with subsequent somatic diseases and premature death. *JAMA Psychiatry*. 2021;78(3):302-10. doi: 10.1001/jamapsychiatry.2020.3786.
- 20. Bufferd SJ, Dougherty LR, Olino TM. Mapping the frequency and severity of depressive behaviors in preschool-aged children. *Child Psychiatry Hum Dev*. 2017 Dec;48(6):934-43. doi: 10.1007/s10578-017-0715-2. PMID: 28281019.
- 21. Luby JL, Heffelfinger AK, Mrakotsky C, et al. Preschool major depressive disorder: preliminary validation for developmentally modified DSM-IV criteria. *J Am Acad Child Adolesc Psychiatry*. 2002 Aug;41(8):928-37. doi: 10.1097/00004583-200208000-00011. PMID: 12162628.
- Whalen DJ, Dixon-Gordon K, Belden AC, et al. Correlates and consequences of suicidal cognitions and behaviors in children ages 3 to 7 years. *J Am Acad Child Adolesc Psychiatry*. 2015 Nov;54(11):926-37.e2. doi: 10.1016/j.jaac.2015.08.009. PMID: 26506583.
- 23. Nock MK, Green JG, Hwang I, et al. Prevalence, correlates, and treatment of lifetime suicidal behavior among adolescents: results from the National Comorbidity Survey Replication Adolescent Supplement. *JAMA Psychiatry*. 2013 Mar;70(3):300-10. doi: 10.1001/2013.jamapsychiatry.55. PMID: 23303463.
- 24. Sampasa-Kanyinga H, Dupuis LC, Ray R. Prevalence and correlates of suicidal ideation and attempts among children and adolescents. *Int J Adolesc Med Health*. 2017 Apr 1;29(2)doi: 10.1515/ijamh-2015-0053. PMID: 26556839.
- 25. Mars B, Heron J, Klonsky ED, et al. Predictors of future suicide attempt among adolescents with suicidal thoughts or non-suicidal self-harm: a population-based birth cohort study. *Lancet Psychiatry*. 2019 Apr;6(4):327-37. doi: 10.1016/s2215-0366(19)30030-6. PMID: 30879972.
- 26. Kessler RC. National comorbidity survey: adolescent supplement (NCS-A), 2001-2004: Inter-university Consortium for Political and Social Research; 2011.
- 27. Kessler RC, Avenevoli S, Costello EJ, et al. Prevalence, persistence, and sociodemographic correlates of DSM-IV disorders in the National Comorbidity Survey Replication Adolescent Supplement. *Arch Gen Psychiatry*. 2012 Apr;69(4):372-80. doi: 10.1001/archgenpsychiatry.2011.160. PMID: 22147808.

- 28. Substance Abuse and Mental Health Services Administration. *Results from the 2011 National Survey on Drug Use and Health: Mental Health Findings.* NSDUH Series H-45, HHS Publication No. (SMA) 12-4725 Substance Abuse and Mental Health Services Administration. Rockville, MD: 2012.
- 29. National Institute of Mental Health. Suicide prevention. Bethesda, MD: National Institute of Mental Health; 2019. https://www.nimh.nih.gov/health/topics/suicide-prevention/index.shtml. Accessed April 6, 2021.
- 30. Miron O, Yu KH, Wilf-Miron R, et al. Suicide rates among adolescents and young adults in the United States, 2000-2017. *JAMA*. 2019 Jun 18;321(23):2362-4. doi: 10.1001/jama.2019.5054. PMID: 31211337.
- 31. Twenge JM, Joiner TE, Rogers ML, et al. Increases in depressive symptoms, suicide-related outcomes, and suicide rates among US adolescents after 2010 and links to increased new media screen time. *Clin Psychol Sci.* 2018;6(1):3-17. doi: 10.1177/2167702617723376. PMID: 2017-58243-001.
- 32. Haas AP, Eliason M, Mays VM, et al. Suicide and suicide risk in lesbian, gay, bisexual, and transgender populations: review and recommendations. *J Homosex*. 2010;58(1):10-51.
- 33. Marshal MP, Dermody SS, Shultz ML, et al. Mental health and substance use disparities among urban adolescent lesbian and bisexual girls. *J Am Psychiatr Nurses Assoc*. 2013 Sep-Oct;19(5):271-9. doi: 10.1177/1078390313503552. PMID: 24055956.
- 34. Hatchel T, Espelage DL, Huang Y. Sexual harassment victimization, school belonging, and depressive symptoms among LGBTQ adolescents: temporal insights. *Am J Orthopsychiatry*. 2018;88(4):422-30. doi: 10.1037/ort0000279. PMID: 2017-26162-001.
- 35. Peyre H, Hoertel N, Stordeur C, et al. Contributing factors and mental health outcomes of first suicide attempt during childhood and adolescence: results from a nationally representative study. *J Clin Psychiatry*. 2017 Jun;78(6):e622-e30. doi: 10.4088/JCP.16m10876. PMID: 28355042.
- 36. Zubrick SR, Hafekost J, Johnson SE, et al. The continuity and duration of depression and its relationship to non-suicidal self-harm and suicidal ideation and behavior in adolescents 12-17. *J Affect Disord*. 2017 Oct 1;220:49-56. doi: 10.1016/j.jad.2017.05.050. PMID: 28595098.
- 37. Gomez SH, Tse J, Wang Y, et al. Are there sensitive periods when child maltreatment substantially elevates suicide risk? Results from a nationally representative sample of adolescents. *Depress Anxiety*. 2017 Aug;34(8):734-41. doi: 10.1002/da.22650. PMID: 28544045.
- 38. Winsper C, Lereya T, Zanarini M, et al. Involvement in bullying and suicide-related behavior at 11 years: a prospective birth cohort study. *J Am Acad Child Adolesc Psychiatry*. 2012 Mar;51(3):271-82.e3. doi: 10.1016/j.jaac.2012.01.001. PMID: 22365463.
- 39. Pyke JE, Murphy EM. Australian health and fitness survey 1985: the fitness, health and physical performance of Australian school students aged 7-15 years: Australian Council for Health, Physical Education and Recreation; 1987.
- 40. Auerbach RP, Stewart JG, Johnson SL. Impulsivity and suicidality in adolescent inpatients. *J Abnorm Child Psychol*. 2017 Jan;45(1):91-103. doi: 10.1007/s10802-016-0146-8. PMID: 27025937.

- 41. Kasen S, Cohen P, Chen H. Developmental course of impulsivity and capability from age 10 to age 25 as related to trajectory of suicide attempt in a community cohort. *Suicide Life Threat Behav*. 2011 Apr;41(2):180-92. doi: 10.1111/j.1943-278X.2011.00017.x. PMID: 21342218.
- 42. Stewart JG, Esposito EC, Glenn CR, et al. Adolescent self-injurers: comparing non-ideators, suicide ideators, and suicide attempters. *J Psychiatr Res*. 2017 Jan;84:105-12. doi: 10.1016/j.jpsychires.2016.09.031. PMID: 27716512.
- 43. Mann JJ. Neurobiology of suicidal behaviour. *Nat Rev Neurosci*. 2003 Oct;4(10):819-28. doi: 10.1038/nrn1220. PMID: 14523381.
- 44. Xiao Y, Romanelli M, Lindsey MA. A latent class analysis of health lifestyles and suicidal behaviors among US adolescents. *J Affect Disord*. 2019 Aug 1;255:116-26. doi: 10.1016/j.jad.2019.05.031. PMID: 31150941.
- 45. Essau CA, Lewinsohn PM, Lim JX, et al. Incidence, recurrence and comorbidity of anxiety disorders in four major developmental stages. *J Affect Disord*. 2018 Mar 1;228:248-53. doi: 10.1016/j.jad.2017.12.014. PMID: 29304469.
- 46. Beesdo-Baum K, Hofler M, Gloster AT, et al. The structure of common mental disorders: a replication study in a community sample of adolescents and young adults. *Int J Methods Psychiatr Res.* 2009 Dec;18(4):204-20. doi: 10.1002/mpr.293. PMID: 20024895.
- 47. Tandon M, Cardeli E, Luby J. Internalizing disorders in early childhood: a review of depressive and anxiety disorders. *Child Adolesc Psychiatr Clin N Am.* 2009 Jul;18(3):593-610. doi: 10.1016/j.chc.2009.03.004. PMID: 19486840.
- 48. Beesdo K, Bittner A, Pine DS, et al. Incidence of social anxiety disorder and the consistent risk for secondary depression in the first three decades of life. *Arch Gen Psychiatry*. 2007 Aug;64(8):903-12. doi: 10.1001/archpsyc.64.8.903. PMID: 17679635.
- 49. Ehrenreich JT, Santucci LC, Weiner CL. Separation anxiety disorder in youth: Phenomenology, assessment, and treatment. *Behavioral Psychology*. 2008;16(3):389-412. PMID: 2014-29992-003.
- 50. Riordan DM, Singhal D. Anxiety-related disorders: an overview. *J Paediatr Child Health*. 2018 Oct;54(10):1104-9. doi: 10.1111/jpc.14167. PMID: 30294986.
- 51. Beesdo K, Pine DS, Lieb R, et al. Incidence and risk patterns of anxiety and depressive disorders and categorization of generalized anxiety disorder. *Arch Gen Psychiatry*. 2010 Jan;67(1):47-57. doi: 10.1001/archgenpsychiatry.2009.177. PMID: 20048222.
- 52. Yap MB, Jorm AF. Parental factors associated with childhood anxiety, depression, and internalizing problems: a systematic review and meta-analysis. *J Affect Disord*. 2015 Apr 1;175:424-40. doi: 10.1016/j.jad.2015.01.050. PMID: 25679197.
- 53. Lemstra M, Neudorf C, D'Arcy C, et al. A systematic review of depressed mood and anxiety by SES in youth aged 10–15 years. *Can J Public Health*. 2008;99(2):125-9.
- 54. Knappe S, Beesdo-Baum K, Fehm L, et al. Social fear and social phobia types among community youth: differential clinical features and vulnerability factors. *J Psychiatr Res*. 2011 Jan;45(1):111-20. doi: 10.1016/j.jpsychires.2010.05.002. PMID: 20684833.
- 55. Laurin CA, Hottenga JJ, Willemsen G, et al. Genetic analyses benefit from using less heterogeneous phenotypes: an illustration with the hospital anxiety and depression scale (HADS). *Genet Epidemiol*. 2015 May;39(4):317-24. doi: 10.1002/gepi.21897. PMID: 25832296.

- 56. Kagan J, Reznick JS, Snidman N. Biological bases of childhood shyness. *Science*. 1988 Apr 8;240(4849):167-71. doi: 10.1126/science.3353713. PMID: 3353713.
- 57. Hyde JS, Mezulis AH, Abramson LY. The ABCs of depression: integrating affective, biological, and cognitive models to explain the emergence of the gender difference in depression. *Psychol Rev.* 2008 Apr;115(2):291-313. doi: 10.1037/0033-295x.115.2.291. PMID: 18426291.
- 58. Sheftall AH, Asti L, Horowitz LM, et al. Suicide in elementary school-aged children and early adolescents. *Pediatrics*. 2016 Oct;138(4)doi: 10.1542/peds.2016-0436. PMID: 27647716.
- 59. Beesdo-Baum K, Knappe S, Asselmann E, et al. The 'Early Developmental Stages of Psychopathology (EDSP) study': a 20-year review of methods and findings. *Soc Psychiatry Psychiatr Epidemiol*. 2015 Jun;50(6):851-66. doi: 10.1007/s00127-015-1062-x. PMID: 25982479.
- 60. Bogels SM, Brechman-Toussaint ML. Family issues in child anxiety: attachment, family functioning, parental rearing and beliefs. *Clin Psychol Rev*. 2006 Nov;26(7):834-56. doi: 10.1016/j.cpr.2005.08.001. PMID: 16473441.
- 61. Bufferd SJ, Dougherty LR, Carlson GA, et al. Parent-reported mental health in preschoolers: findings using a diagnostic interview. *Compr Psychiatry*. 2011 Jul-Aug;52(4):359-69. doi: 10.1016/j.comppsych.2010.08.006. PMID: 21683173.
- 62. Bufferd SJ, Dougherty LR, Carlson GA, et al. Psychiatric disorders in preschoolers: continuity from ages 3 to 6. *Am J Psychiatry*. 2012 Nov;169(11):1157-64. doi: 10.1176/appi.ajp.2012.12020268. PMID: 23128922.
- 63. Luby JL, Gaffrey MS, Tillman R, et al. Trajectories of preschool disorders to full DSM depression at school age and early adolescence: continuity of preschool depression. *Am J Psychiatry*. 2014 Jul;171(7):768-76. doi: 10.1176/appi.ajp.2014.13091198. PMID: 24700355.
- 64. Costello EJ, Copeland W, Angold A. Trends in psychopathology across the adolescent years: what changes when children become adolescents, and when adolescents become adults? *J Child Psychol Psychiatry*. 2011 Oct;52(10):1015-25. doi: 10.1111/j.1469-7610.2011.02446.x. PMID: 21815892.
- 65. Rohde P, Lewinsohn PM, Klein DN, et al. Key characteristics of major depressive disorder occurring in childhood, adolescence, emerging adulthood, adulthood. *Clin Psychol Sci.* 2013 Jan;1(1)doi: 10.1177/2167702612457599. PMID: 24273703.
- 66. Hankin BL. Depression from childhood through adolescence: risk mechanisms across multiple systems and levels of analysis. *Curr Opin Psychol*. 2015 Aug;4:13-20. doi: 10.1016/j.copsyc.2015.01.003. PMID: 25692174.
- 67. Costello EJ, Mustillo S, Erkanli A, et al. Prevalence and development of psychiatric disorders in childhood and adolescence. *Arch Gen Psychiatry*. 2003 Aug;60(8):837-44. doi: 10.1001/archpsyc.60.8.837. PMID: 12912767.
- 68. Wilson S, Hicks BM, Foster KT, et al. Age of onset and course of major depressive disorder: associations with psychosocial functioning outcomes in adulthood. *Psychol Med.* 2015 Feb;45(3):505-14. doi: 10.1017/s0033291714001640. PMID: 25007761.
- 69. Franz L, Angold A, Copeland W, et al. Preschool anxiety disorders in pediatric primary care: prevalence and comorbidity. *J Am Acad Child Adolesc Psychiatry*. 2013 Dec;52(12):1294-303.e1. doi: 10.1016/j.jaac.2013.09.008. PMID: 24290462.

- 70. Cicchetti D, Lynch M. Toward an ecological/transactional model of community violence and child maltreatment: consequences for children's development. *Psychiatry*. 1993 Feb;56(1):96-118. doi: 10.1080/00332747.1993.11024624. PMID: 8488217.
- 71. Shortt AL, Spence SH. Risk and protective factors for depression in youth. *Behav Change*. 2006;23(1):1-30.
- 72. Sullivan PF, Neale MC, Kendler KS. Genetic epidemiology of major depression: review and meta-analysis. *Am J Psychiatry*. 2000 Oct;157(10):1552-62. doi: 10.1176/appi.ajp.157.10.1552. PMID: 11007705.
- 73. Saluja G, Iachan R, Scheidt PC, et al. Prevalence of and risk factors for depressive symptoms among young adolescents. *Arch Pediatr Adolesc Med.* 2004 Aug;158(8):760-5. doi: 10.1001/archpedi.158.8.760. PMID: 15289248.
- 74. Shore L, Toumbourou JW, Lewis AJ, et al. Longitudinal trajectories of child and adolescent depressive symptoms and their predictors—a systematic review and meta-analysis. *Child Adolesc Ment Health*. 2018;23(2):107-20.
- 75. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *Am J Psychiatry*. 2012 Feb;169(2):141-51. doi: 10.1176/appi.ajp.2011.11020335. PMID: 22420036.
- 76. Maughan B, Collishaw S, Stringaris A. Depression in childhood and adolescence. *J Can Acad Child Adolesc Psychiatry*. 2013 Feb;22(1):35-40. PMID: 23390431.
- 77. Thapar A, Collishaw S, Pine DS, et al. Depression in adolescence. *Lancet*. 2012 Mar 17;379(9820):1056-67. doi: 10.1016/s0140-6736(11)60871-4. PMID: 22305766.
- 78. Hariri AR, Mattay VS, Tessitore A, et al. Serotonin transporter genetic variation and the response of the human amygdala. *Science*. 2002 Jul 19;297(5580):400-3. doi: 10.1126/science.1071829. PMID: 12130784.
- 79. Heron M. Deaths: leading causes for 2019 National Center for Health Statistics. Hyattsville, MD: 2021.
- 80. Centers for Disease Control and Prevention. WISQARS. https://wisqars.cdc.gov/data/explore-data/home.
- 81. Sheftall AH, Vakil F, Ruch DA, et al. Black youth suicide: investigation of current trends and precipitating circumstances. *J Am Acad Child Adolesc Psychiatry*. 2021doi: 10.1016/j.jaac.2021.08.021. PMID: 34509592.
- 82. Ream GL. What's unique about lesbian, gay, bisexual, and transgender (LGBT) youth and young adult suicides? Findings from the National Violent Death Reporting System. *J Adolesc Health*. 2019;64(5):602-7. doi: 10.1016/j.jadohealth.2018.10.303. PMID: 2019-05735-001.
- 83. Kann L, McManus T, Harris WA, et al. Youth risk behavior surveillance—United States, 2017. *MMWR Surveill Summ*. 2018;67(8):1.
- 84. The Trevor Project. 2021 National Survey on LGBTQ Youth Mental Health The Trevor Project. West Hollywood, CA: 2021.
- 85. Toomey RB, Syvertsen AK, Shramko M. Transgender adolescent suicide behavior. *Pediatrics*. 2018 Oct;142(4)doi: 10.1542/peds.2017-4218. PMID: 30206149.
- 86. Basile K, Clayton H, DeGue S, et al. Interpersonal violence victimization among high school students—Youth Risk Behavior Survey, United States, 2019. *MMWR Supplements*. 2020;69(1):28.
- 87. DeVille DC, Whalen D, Breslin FJ, et al. Prevalence and family-related factors associated with suicidal ideation, suicide attempts, and self-injury in children aged 9 to 10 years.

- *JAMA Netw Open.* 2020 Feb 5;3(2):e1920956. doi: 10.1001/jamanetworkopen.2019.20956. PMID: 32031652.
- 88. Jones JD, Boyd RC, Calkins ME, et al. Parent-adolescent agreement about adolescents' suicidal thoughts. *Pediatrics*. 2019 Feb;143(2)doi: 10.1542/peds.2018-1771. PMID: 30642950.
- 89. U.S. Department of Commerce. 2020 National Survey of Children's Health: topical frequencies U.S. Census Bureau. Washington, DC: 2021.
- 90. Ghandour RM, Sherman LJ, Vladutiu CJ, et al. Prevalence and treatment of depression, anxiety, and conduct problems in US children. *J Pediatr*. 2019 Mar;206:256-67.e3. doi: 10.1016/j.jpeds.2018.09.021. PMID: 30322701.
- 91. Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2019 National Survey on Drug Use and Health Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Rockville, MD: 2020.
- 92. Manzo K, Tiesman H, Stewart J, et al. A comparison of risk factors associated with suicide ideation/attempts in American Indian and white youth in Montana. *Arch Suicide Res.* 2015;19(1):89-102. doi: 10.1080/13811118.2013.840254. PMID: 25010183.
- 93. Bridge JA, Horowitz LM, Fontanella CA, et al. Age-related racial disparity in suicide rates among US youths from 2001 through 2015. *JAMA Pediatr*. 2018 Jul 1;172(7):697-9. doi: 10.1001/jamapediatrics.2018.0399. PMID: 29799931.
- 94. Bridge JA, Asti L, Horowitz LM, et al. Suicide trends among elementary school–aged children in the United States from 1993 to 2012. *JAMA Pediatr*. 2015;169(7):673-7. doi: 10.1001/jamapediatrics.2015.0465.
- 95. Lindsey MA, Sheftall AH, Xiao Y, et al. Trends of suicidal behaviors among high school students in the United States: 1991–2017. *Pediatrics*. 2019;144(5)doi: 10.1542/peds.2019-1187. PMID: 2019-77312-001.
- 96. Louie P, Wheaton B. Prevalence and patterning of mental disorders through adolescence in 3 cohorts of black and white Americans. *Am J Epidemiol*. 2018 Nov 1;187(11):2332-8. doi: 10.1093/aje/kwy144. PMID: 29992256.
- 97. Alegría M, Green JG, McLaughlin KA, et al. Disparities in child and adolescent mental health and mental health services in the US. *New York, NY: William T. Grant Foundation*. 2015.
- 98. Ettman CK, Cohen GH, Abdalla SM, et al. Do assets explain the relation between race/ethnicity and probable depression in U.S. adults? *PLoS One*. 2020;15(10):e0239618. doi: 10.1371/journal.pone.0239618. PMID: 33006988.
- 99. Assari S, Caldwell CH. High risk of depression in high-income African American boys. *J Racial Ethn Health Disparities*. 2018 Aug;5(4):808-19. doi: 10.1007/s40615-017-0426-1. PMID: 28842841.
- 100. Assari S, Gibbons FX, Simons R. Depression among black youth; interaction of class and place. *Brain Sci.* 2018 Jun 12;8(6)doi: 10.3390/brainsci8060108. PMID: 29895752.
- 101. Yeh M, McCabe K, Hurlburt M, et al. Referral sources, diagnoses, and service types of youth in public outpatient mental health care: a focus on ethnic minorities. *J Behav Health Serv Res*. 2002 Feb;29(1):45-60. doi: 10.1007/bf02287831. PMID: 11840904.
- 102. Bailey RK, Mokonogho J, Kumar A. Racial and ethnic differences in depression: current perspectives. *Neuropsychiatr Dis Treat*. 2019;15:603-9. doi: 10.2147/ndt.S128584. PMID: 30863081.

- 103. Fadus MC, Ginsburg KR, Sobowale K, et al. Unconscious bias and the diagnosis of disruptive behavior disorders and ADHD in African American and Hispanic youth. *Acad Psychiatry*. 2020 Feb;44(1):95-102. doi: 10.1007/s40596-019-01127-6. PMID: 31713075.
- 104. Liang J, Matheson BE, Douglas JM. Mental health diagnostic considerations in racial/ethnic minority youth. *J Child Fam Stud*. 2016 Jun;25(6):1926-40. doi: 10.1007/s10826-015-0351-z. PMID: 27346929.
- 105. Bernard DL, Calhoun CD, Banks DE, et al. Making the "C-ACE" for a Culturally-informed Adverse Childhood Experiences framework to understand the pervasive mental health impact of racism on black youth. *J Child Adolesc Trauma*. 2021 Jun;14(2):233-47. doi: 10.1007/s40653-020-00319-9. PMID: 33986909.
- 106. Lu W. Treatment for adolescent depression: national patterns, temporal trends, and factors related to service use across settings. *J Adolesc Health*. 2020;67(3):401-8. doi: 10.1016/j.jadohealth.2020.02.019. PMID: 32331929.
- 107. Lu W. Child and adolescent mental disorders and health care disparities: results from the National Survey of Children's Health, 2011-2012. *J Health Care Poor Underserved*. 2017;28(3):988-1011. doi: 10.1353/hpu.2017.0092. PMID: 28804073.
- 108. Merikangas KR, He JP, Burstein M, et al. Service utilization for lifetime mental disorders in U.S. adolescents: results of the National Comorbidity Survey-Adolescent Supplement (NCS-A). *J Am Acad Child Adolesc Psychiatry*. 2011 Jan;50(1):32-45. doi: 10.1016/j.jaac.2010.10.006. PMID: 21156268.
- 109. Howell E, McFeeters J. Children's mental health care: differences by race/ethnicity in urban/rural areas. *J Health Care Poor Underserved*. 2008 Feb;19(1):237-47. doi: 10.1353/hpu.2008.0008. PMID: 18263999.
- 110. Emergency TaskForce on Black Youth Suicide and Mental Health. Ring the alarm: The crisis of Black youth suicide in America. 2019. https://watsoncoleman.house.gov/uploadedfiles/full_taskforce_report.pdf
- 111. Pavkov TW, Travis L, Fox KA, et al. Tribal youth victimization and delinquency: analysis of Youth Risk Behavior Surveillance Survey data. *Cultur Divers Ethnic Minor Psychol*. 2010 Apr;16(2):123-34. doi: 10.1037/a0018664. PMID: 20438150.
- 112. Garcia JL. Historical trauma and American Indian/Alaska Native youth mental health development and delinquency. *New Dir Child Adolesc Dev.* 2020 Jan;2020(169):41-58. doi: 10.1002/cad.20332. PMID: 32324321.
- 113. Kessler RC, Avenevoli S, Ries Merikangas K. Mood disorders in children and adolescents: an epidemiologic perspective. *Biol Psychiatry*. 2001 Jun 15;49(12):1002-14. doi: 10.1016/s0006-3223(01)01129-5. PMID: 11430842.
- 114. Kramer T, Iliffe S, Murray E, et al. Which adolescents attend the GP? *Br J Gen Pract*. 1997 May;47(418):327. PMID: 9219415.
- 115. Kramer T, Garralda ME. Psychiatric disorders in adolescents in primary care. *Br J Psychiatry*. 1998 Dec;173:508-13. doi: 10.1192/bjp.173.6.508. PMID: 9926080.
- 116. Yates P, Kramer T, Garralda E. Depressive symptoms amongst adolescent primary care attenders. Levels and associations. *Soc Psychiatry Psychiatr Epidemiol*. 2004 Jul;39(7):588-94. doi: 10.1007/s00127-004-0792-y. PMID: 15243698.
- 117. Ahmedani BK, Simon GE, Stewart C, et al. Health care contacts in the year before suicide death. *J Gen Intern Med*. 2014 Jun;29(6):870-7. doi: 10.1007/s11606-014-2767-3. PMID: 24567199.

- 118. Martini R, Hilt R, Marx L, et al. Best principles for integration of child psychiatry into the pediatric health home. Washington, DC: American Academy of Child & Adolescent Psychiatry; 2012.
- 119. O'Connor E, Gaynes BN, Burda BU, et al. Screening for and treatment of suicide risk relevant to primary care: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2013 May 21;158(10):741-54. doi: 10.7326/0003-4819-158-10-201305210-00642. PMID: 23609101.
- 120. Substance Abuse and Mental Health Services Administration. Treatment for suicidal ideation, self-harm, and suicide attempts among youth National Mental Health and Substance Use Policy Laboratory. Substance Abuse and Mental Health Services Administration. Rockville, MD: 2020.
- 121. Robinson J, Bailey E, Witt K, et al. What works in youth suicide prevention? A systematic review and meta-analysis. *EClinicalMedicine*. 2018 Oct-Nov;4-5:52-91. doi: 10.1016/j.eclinm.2018.10.004. PMID: 31193651.
- 122. Morken IS, Dahlgren A, Lunde I, et al. The effects of interventions preventing self-harm and suicide in children and adolescents: an overview of systematic reviews. *F1000Research*. 2020;8doi: 10.12688/f1000research.19506.2.
- 123. Wang Z, Whiteside S, Sim L, et al. Anxiety in children Comparative Effectiveness Reviews No. 192. (Prepared by the Mayo Clinic Evidence-based Practice Center under Contract No. 290-2015-00013-I.). Report No.: 17-EHC023-EF. Rockville, MD: Agency for Healthcare Research and Quality; Aug 2017.

 www.effectivehealthcare.ahrq.gov/reports/final.cfm
- 124. Wehry AM, Beesdo-Baum K, Hennelly MM, et al. Assessment and treatment of anxiety disorders in children and adolescents. *Curr Psychiatry Rep.* 2015 Jul;17(7):52. doi: 10.1007/s11920-015-0591-z. PMID: 25980507.
- 125. Connolly SD, Suarez L, Sylvester C. Assessment and treatment of anxiety disorders in children and adolescents. *Curr Psychiatry Rep.* 2011 Apr;13(2):99-110. doi: 10.1007/s11920-010-0173-z. PMID: 21225481.
- 126. Comer JS, Hong N, Poznanski B, et al. Evidence base update on the treatment of early childhood anxiety and related problems. *J Clin Child Adolesc Psychol*. 2019 Jan-Feb;48(1):1-15. doi: 10.1080/15374416.2018.1534208. PMID: 30640522.
- 127. Higa-McMillan CK, Francis SE, Rith-Najarian L, et al. Evidence base update: 50 years of research on treatment for child and adolescent anxiety. *J Clin Child Adolesc Psychol*. 2016;45(2):91-113. doi: 10.1080/15374416.2015.1046177. PMID: 26087438.
- 128. March J, Silva S, Petrycki S, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA*. 2004 Aug 18;292(7):807-20. doi: 10.1001/jama.292.7.807. PMID: 15315995.
- 129. Pampallona S, Bollini P, Tibaldi G, et al. Combined pharmacotherapy and psychological treatment for depression: a systematic review. *Arch Gen Psychiatry*. 2004 Jul;61(7):714-9. doi: 10.1001/archpsyc.61.7.714. PMID: 15237083.
- 130. Ruch DA, Sheftall AH, Schlagbaum P, et al. Trends in suicide among youth aged 10 to 19 years in the United States, 1975 to 2016. *JAMA network open.* 2019;2(5):e193886-e.
- 131. David-Ferdon C, Kaslow NJ. Evidence-based psychosocial treatments for child and adolescent depression. *J Clin Child Adolesc Psychol*. 2008 Jan;37(1):62-104. doi: 10.1080/15374410701817865. PMID: 18444054.

- 132. Merry SN, Stasiak K, Shepherd M, et al. The effectiveness of SPARX, a computerised self help intervention for adolescents seeking help for depression: randomised controlled non-inferiority trial. *BMJ*. 2012;344:e2598. doi: 10.1136/bmj.e2598. PMID: 22517917.
- 133. Mufson L, Sills R. Interpersonal psychotherapy for depressed adolescents (IPT-A): an overview. *Nord J Psychiatry*. 2006;60(6):431-7. doi: 10.1080/08039480601022397. PMID: 17162450.
- 134. Cheung AH, Zuckerbrot RA, Jensen PS, et al. Guidelines for adolescent depression in primary care (GLAD-PC): II. treatment and ongoing management. *Pediatrics*. 2007 Nov;120(5):e1313-26. doi: 10.1542/peds.2006-1395. PMID: 17974724.
- 135. Centers for Medicare & Medicaid Services. Antidepressant medications: U.S. Food and Drug Administration-approved indications and dosages for use in pediatric patients. Baltimore, MD: Centers for Medicare & Medicaid Services; 2015. https://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/Medicaid-Integrity-Education/Pharmacy-Education-Materials/Downloads/ad-pediatric-dosingchart11-14.pdf. Accessed March 3, 2020.
- 136. Romer D, McIntosh M. Chapter 31. The role of primary care physicians in detection and treatment of adolescent mental health problems. In: Evans DL, Foa EB, Gur RE, Hendin H, O'Brien CP, Romer D, et al., eds. Treating and preventing adolescent mental health disorders: what we know and what we don't know: A research agenda for improving the mental health of our youthd. 2nd ed. New York, NY: Oxford University Press; 2012.
- 137. Zenlea IS, Milliren CE, Mednick L, et al. Depression screening in adolescents in the United States: a national study of ambulatory office-based practice. *Acad Pediatr*. 2014 Mar-Apr;14(2):186-91. doi: 10.1016/j.acap.2013.11.006. PMID: 24602582.
- 138. Deepa L Sekhar, Djibril M Ba, Guodong Liu, et al. Major depressive disorder screening remains low even among privately insured adolescents. *J Pediatr*. 2019;204:203-7. doi: 10.1016/j.jpeds.2018.07.086.
- 139. Habis A, Tall L, Smith J, et al. Pediatric emergency medicine physicians' current practices and beliefs regarding mental health screening. *Pediatr Emerg Care*. 2007 Jun;23(6):387-93. doi: 10.1097/01.pec.0000278401.37697.79. PMID: 17572523.
- 140. Frankenfield DL, Keyl PM, Gielen A, et al. Adolescent patients--healthy or hurting? Missed opportunities to screen for suicide risk in the primary care setting. *Arch Pediatr Adolesc Med.* 2000 Feb;154(2):162-8. doi: 10.1001/archpedi.154.2.162. PMID: 10665603.
- 141. American Academy of Family Physicians. Summary of recommendations for clinical preventive services. Leawood, KS: American Academy of Family Physicians; 2017. https://www.aafp.org/dam/AAFP/documents/patient_care/clinical_recommendations/cps-recommendations.pdf. Accessed April 19, 2021.
- 142. American Academy of Pediatrics. Screening for suicide risk in clinical practice. American Academy of Pediatrics; 2022. https://www.aap.org/en/patient-care/blueprint-for-youth-suicide-prevention/strategies-for-clinical-settings-for-youth-suicide-prevention/screening-for-suicide-risk-in-clinical-practice/. Accessed April 8, 2022.
- 143. American Academy of Child and Adolescent Psychiatry. Policy statement on suicide prevention. Washington, DC: American Academy of Child and Adolescent Psychiatry; 2019. Accessed April 19, 2021.

- 144. The Joint Commission. National Patient Safety Goal for suicide prevention. 2019. https://www.jointcommission.org/-/media/tjc/documents/standards/r3-reports/r3-18-suicide-prevention-hap-bhc-cah-11-4-19-final1.pdf
- 145. Walter HJ, Bukstein OG, Abright AR, et al. Clinical practice guideline for the assessment and treatment of children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2020 Oct;59(10):1107–24. doi: 10.1016/j.jaac.2020.05.005. PMID: 32439401.
- 146. National Institute for Health and Care Excellence (NICE). Assessment of children and young people with possible social anxiety disorder. London: National Institute for Health and Care Excellence; 2013. https://www.nice.org.uk/guidance/cg159/chapter/1-Recommendations#identification-and-assessment-of-children-and-young-people. Accessed April 29, 2021.
- 147. Zuckerbrot RA, Cheung A, Jensen PS, et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): part I. Practice preparation, identification, assessment, and initial management. *Pediatrics*. 2018 Mar;141(3)doi: 10.1542/peds.2017-4081. PMID: 29483200.
- 148. Beck A, LeBlanc JC, Morissette K, et al. Screening for depression in children and adolescents: a protocol for a systematic review update. *Syst Rev.* 2021 Jan 12;10(1):24. doi: 10.1186/s13643-020-01568-3. PMID: 33436094.
- 149. MacMillan HL, Patterson CJ, Wathen CN, et al. Screening for depression in primary care: recommendation statement from the Canadian Task Force on Preventive Health Care. *CMAJ*. 2005 Jan 4;172(1):33-5. doi: 10.1503/cmaj.1030823. PMID: 15632399.
- 150. Weitzman C, Wegner L. Promoting optimal development: screening for behavioral and emotional problems. *Pediatrics*. 2015 Feb;135(2):384-95. doi: 10.1542/peds.2014-3716. PMID: 25624375.
- 151. American College of Obstetricians and Gynecologists (ACOG). Mental health disorders in adolescents. Washington, DC: American College of Obstetricians and Gynecologists; 2017. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2017/07/mental-health-disorders-in-adolescents. Accessed April 19, 2021.
- 152. Forman-Hoffman V, McClure E, McKeeman J, et al. Screening for major depressive disorder in children and adolescents: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2016 Mar 1;164(5):342-9. doi: 10.7326/m15-2259. PMID: 26857836.
- 153. Viswanathan M, Kennedy SM, McKeeman J, et al. Treatment of depression in children and adolescents: a systematic review AHRQ Comparative Effectiveness Review Number 224. AHRQ Publication No. 20-EHC005-EF. Rockville (MD): Agency for Healthcare Research and Quality; April 2020.
- 154. United Nations Development Programme. Human development report 2019. New York, NY: United Nations Development Programme; 2019. http://hdr.undp.org/sites/default/files/hdr2019.pdf. Accessed April 6, 2021.
- 155. Sterne JAC, Savovic J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019 Aug 28;366:14898. doi: 10.1136/bmj.14898. PMID: 31462531.

- 156. Sterne JA, Hernan MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016 Oct 12;355:i4919. doi: 10.1136/bmj.i4919. PMID: 27733354.
- 157. Whiting P, Savovic J, Higgins JP, et al. ROBIS: a new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol*. 2016 Jan;69:225-34. doi: 10.1016/j.jclinepi.2015.06.005. PMID: 26092286.
- 158. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med.* 2011 Oct 18;155(8):529-36. doi: 10.7326/0003-4819-155-8-201110180-00009. PMID: 22007046.
- 159. U.S. Preventive Services Task Force. Appendix VI. Criteria for assessing internal validity of individual studies. In Procedure Manual. Rockville, MD: U.S. Preventive Services Task Force; 2015. https://www.uspreventiveservicestaskforce.org/Page/Name/appendix-vi-criteria-for-assessing-internal-validity-of-individual-studies.
- 160. West SL, Gartlehner G, Mansfield AJ, et al. Comparative effectiveness review methods: clinical heterogeneity. 10-EHC070-EF. Rockville, MD: Agency for Healthcare Research and Quality; Sep 2010. https://www.ncbi.nlm.nih.gov/pubmed/21433337
- 161. Deeks JJ, Higgins JPT, Altman DG, et al. Chapter 10: analysing data and undertaking meta-analyses. 10.10 Heterogeneity. 10.10.1 What is heterogeneity? London: Cochrane Training. https://training.cochrane.org/handbook/current/chapter-10#section-10-10. Accessed April 6, 2021.
- 162. Borenstein M, Hedges L, Higgins J, et al. Comprehensive meta-analysis version 3. Englewood, NJ: Biostat; 2013.
- 163. Arendt K, Thastum M, Hougaard E. Efficacy of a Danish version of the Cool Kids program: a randomized wait-list controlled trial. *Acta Psychiatr Scand.* 2016;133(2):109-21. doi: 10.1111/acps.12448. PMID: 2016-00713-002.
- 164. Asarnow JR, Hughes JL, Babeva KN, et al. Cognitive-behavioral family treatment for suicide attempt prevention: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2017 Jun;56(6):506-14. doi: 10.1016/j.jaac.2017.03.015. PMID: 28545756.
- 165. Asbrand J, Heinrichs N, Schmidtendorf S, et al. Experience versus report: where are changes seen after exposure-based cognitive-behavioral therapy? A randomized controlled group treatment of childhood social anxiety disorder. *Child Psychiatry Hum Dev.* 2020 Jan 20doi: 10.1007/s10578-019-00954-w. PMID: 31960175.
- 166. Bailey KA, Chavira DA, Stein MT, et al. Brief measures to screen for social phobia in primary care pediatrics. *J Pediatr Psychol*. 2006 Jun;31(5):512-21. doi: 10.1093/jpepsy/jsj044. PMID: 16034004.
- 167. Barrett PM, Dadds MR, Rapee RM. Family treatment of childhood anxiety: a controlled trial. *J Consult Clin Psychol*. 1996 Apr;64(2):333-42. doi: 10.1037//0022-006x.64.2.333. PMID: 8871418.
- 168. Birmaher B, Axelson DA, Monk K, et al. Fluoxetine for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2003 Apr;42(4):415-23. doi: 10.1097/01.Chi.0000037049.04952.9f. PMID: 12649628.
- 169. Black B, Uhde TW. Treatment of elective mutism with fluoxetine: a double-blind, placebo-controlled study. *J Am Acad Child Adolesc Psychiatry*. 1994 Sep;33(7):1000-6. doi: 10.1097/00004583-199409000-00010. PMID: 7961338.

- 170. Canals J, Blade J, Carbajo G, et al. The Beck Depression Inventory: psychometric characteristics and usefulness in nonclinical adolescents. *Eur J Psychol Assess*. 2001;17(1):63-8.
- 171. Canals J, Hernández-Martínez C, Cosi S, et al. Examination of a cutoff score for the Screen for Child Anxiety Related Emotional Disorders (SCARED) in a non-clinical Spanish population. *J Anxiety Disord*. 2012 Dec;26(8):785-91. doi: 10.1016/j.janxdis.2012.07.008. PMID: 23023158.
- 172. Christensen KS, Haugen W, Sirpal MK, et al. Diagnosis of depressed young people—criterion validity of WHO-5 and HSCL-6 in Denmark and Norway. *Fam Pract*. 2015;32(3):359-63. doi: 10.1093/fampra/cmv011. PMID: 2015-24236-019.
- 173. Cipriani A, Zhou X, Del Giovane C, et al. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network meta-analysis. *Lancet*. 2016 Aug 27;388(10047):881-90. doi: 10.1016/s0140-6736(16)30385-3. PMID: 27289172.
- 174. Clarke GN, Rohde P, Lewinsohn PM, et al. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *J Am Acad Child Adolesc Psychiatry*. 1999 Mar;38(3):272-9. doi: 10.1097/00004583-199903000-00014. PMID: 10087688.
- 175. Clarke G, Debar L, Lynch F, et al. A randomized effectiveness trial of brief cognitive-behavioral therapy for depressed adolescents receiving antidepressant medication. *J Am Acad Child Adolesc Psychiatry*. 2005 Sep;44(9):888-98. PMID: 16113617.
- 176. Clarke G, DeBar LL, Pearson JA, et al. Cognitive behavioral therapy in primary care for youth declining antidepressants: a randomized trial. *Pediatrics*. 2016 May;137(5). doi: 10.1542/peds.2015-1851. PMID: 27244782.
- 177. Cobham VE, Filus A, Sanders MR. Working with parents to treat anxiety-disordered children: a proof of concept RCT evaluating Fear-less Triple P. *Behav Res Ther*. 2017 Aug;95:128-38. doi: 10.1016/j.brat.2017.06.004. PMID: 28641122.
- 178. Cornacchio D, Furr JM, Sanchez AL, et al. Intensive group behavioral treatment (IGBT) for children with selective mutism: a preliminary randomized clinical trial. *J Consult Clin Psychol*. 2019 Aug;87(8):720-33. doi: 10.1037/ccp0000422. PMID: 31294589.
- 179. Cottrell DJ, Wright-Hughes A, Collinson M, et al. Effectiveness of systemic family therapy versus treatment as usual for young people after self-harm: a pragmatic, phase 3, multicentre, randomised controlled trial. *Lancet Psychiatry*. 2018 Mar;5(3):203-16. doi: 10.1016/s2215-0366(18)30058-0. PMID: 29449180.
- 180. Cottrell DJ, Wright-Hughes A, Collinson M, et al. A pragmatic randomised controlled trial and economic evaluation of family therapy versus treatment as usual for young people seen after second or subsequent episodes of self-harm: the Self-Harm Intervention Family Therapy (SHIFT) trial. *Health Technol Assess*. 2018 Mar;22(12):1-222. doi: 10.3310/hta22120. PMID: 29532784.
- 181. Cottrell DJ, Wright-Hughes A, Eisler I, et al. Longer-term effectiveness of systemic family therapy compared with treatment as usual for young people after self-harm: an extended follow up of pragmatic randomised controlled trial. *EClinicalMedicine*. 2020 Jan;18:100246. doi: 10.1016/j.eclinm.2019.100246. PMID: 31956857.
- 182. Diamond GS, Wintersteen MB, Brown GK, et al. Attachment-based family therapy for adolescents with suicidal ideation: a randomized controlled trial. *J Am Acad Child*

- *Adolesc Psychiatry*. 2010 Feb;49(2):122-31. doi: 10.1097/00004583-201002000-00006. PMID: 20215934.
- 183. Donovan CL, March S. Online CBT for preschool anxiety disorders: a randomised control trial. *Behav Res Ther*. 2014 Jul;58:24-35. doi: 10.1016/j.brat.2014.05.001. PMID: 24927471.
- 184. Ehrenreich-May J, Rosenfield D, Queen AH, et al. An initial waitlist-controlled trial of the unified protocol for the treatment of emotional disorders in adolescents. *J Anxiety Disord*. 2017 Mar;46:46-55. doi: 10.1016/j.janxdis.2016.10.006. PMID: 27771133.
- 185. Emslie GJ, Ventura D, Korotzer A, et al. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry*. 2009 Jul;48(7):721-9. doi: 10.1097/CHI.0b013e3181a2b304. PMID: 19465881.
- 186. Findling RL, Robb A, Bose A. Escitalopram in the treatment of adolescent depression: a randomized, double-blind, placebo-controlled extension trial. *J Child Adolesc Psychopharmacol*. 2013 Sep;23(7):468-80. doi: 10.1089/cap.2012.0023. PMID: 24041408.
- 187. Fristad MA, Vesco AT, Young AS, et al. Pilot randomized controlled trial of omega-3 and individual-family psychoeducational psychotherapy for children and adolescents with depression. *J Clin Child Adolesc Psychol*. 2019;48(sup1):S105-s18. doi: 10.1080/15374416.2016.1233500. PMID: 27819485.
- 188. Garcia-Lopez LJ, Sáez-Castillo AJ, Beidel D, et al. Brief measures to screen for social anxiety in adolescents. *J Dev Behav Pediatr*. 2015 Oct;36(8):562-8. doi: 10.1097/dbp.00000000000213. PMID: 26349070.
- 189. Garrison CZ, Addy CL, Jackson KL, et al. The CES-D as a screen for depression and other psychiatric disorders in adolescents. *J Am Acad Child Adolesc Psychiatry*. 1991 Jul;30(4):636-41. doi: 10.1097/00004583-199107000-00017. PMID: 1890099.
- 190. Ginsburg GS, Pella JE, Pikulski PJ, et al. School-Based Treatment for Anxiety Research Study (STARS): a randomized controlled effectiveness trial. *J Abnorm Child Psychol*. 2020 Mar;48(3):407-17. doi: 10.1007/s10802-019-00596-5. PMID: 31749064.
- 191. Green JM, Wood AJ, Kerfoot MJ, et al. Group therapy for adolescents with repeated self harm: randomised controlled trial with economic evaluation. *BMJ*. 2011 Apr 1;342:d682. doi: 10.1136/bmj.d682. PMID: 21459975.
- 192. Griffiths H, Duffy F, Duffy L, et al. Efficacy of mentalization-based group therapy for adolescents: the results of a pilot randomised controlled trial. *BMC Psychiatry*. 2019 Jun 6;19(1):167. doi: 10.1186/s12888-019-2158-8. PMID: 31170947.
- 193. Hazell PL, Martin G, McGill K, et al. Group therapy for repeated deliberate self-harm in adolescents: failure of replication of a randomized trial. *J Am Acad Child Adolesc Psychiatry*. 2009 Jun;48(6):662-70. doi: 10.1097/CHI.0b013e3181aOacec. PMID: 19454922.
- 194. Hill RM, Pettit JW. Pilot randomized controlled trial of LEAP: a selective preventive intervention to reduce adolescents' perceived burdensomeness. *J Clin Child Adolesc Psychol*. 2019;48:S45-S56. doi: 10.1080/15374416.2016.1188705. PMID: CN-01916512.
- 195. Hirshfeld-Becker DR, Masek B, Henin A, et al. Cognitive behavioral therapy for 4- to 7-year-old children with anxiety disorders: a randomized clinical trial. *J Consult Clin Psychol*. 2010 Aug;78(4):498-510. doi: 10.1037/a0019055. PMID: 20658807.

- 196. Holmes MC, Donovan CL, Farrell LJ, et al. The efficacy of a group-based, disorder-specific treatment program for childhood GAD--a randomized controlled trial. *Behav Res Ther*. 2014 Oct;61:122-35. doi: 10.1016/j.brat.2014.08.002. PMID: 25193003.
- 197. Hooven C, Walsh E, Pike KC, et al. Promoting CARE: including parents in youth suicide prevention. *Fam Community Health*. 2012 Jul-Sep;35(3):225-35. doi: 10.1097/FCH.0b013e318250bcf9. PMID: 22617413.
- 198. Ishikawa SI, Kikuta K, Sakai M, et al. A randomized controlled trial of a bidirectional cultural adaptation of cognitive behavior therapy for children and adolescents with anxiety disorders. *Behav Res Ther*. 2019 Sep;120:103432. doi: 10.1016/j.brat.2019.103432. PMID: 31299461.
- 199. Johnson JG, Harris ES, Spitzer RL, et al. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. *J Adolesc Health*. 2002;30(3):196-204. doi: 10.1016/S1054-139X(01)00333-0. PMID: 2002-02042-008.
- 200. King CA, Klaus N, Kramer A, et al. The Youth-Nominated Support Team-Version II for suicidal adolescents: a randomized controlled intervention trial. *J Consult Clin Psychol*. 2009 Oct;77(5):880-93. doi: 10.1037/a0016552. PMID: 19803568.
- 201. King CA, Arango A, Kramer A, et al. Association of the youth-nominated support team intervention for suicidal adolescents with 11- to 14-year mortality outcomes: secondary analysis of a randomized clinical trial. *JAMA Psychiatry*. 2019 May 1;76(5):492-8. doi: 10.1001/jamapsychiatry.2018.4358. PMID: 30725077.
- 202. King CA, Gipson PY, Horwitz AG, et al. Teen options for change: an intervention for young emergency patients who screen positive for suicide risk. *Psychiatr Serv*. 2015 Jan 1;66(1):97-100. doi: 10.1176/appi.ps.201300347. PMID: 25321886.
- 203. Lau W-y, Chan CK-y, Li JC-h, et al. Effectiveness of group cognitive-behavioral treatment for childhood anxiety in community clinics. *Behav Res Ther*. 2010;48(11):1067-77. doi: 10.1016/j.brat.2010.07.007. PMID: 2010-16900-001.
- 204. Luby JL, Barch DM, Whalen D, et al. A randomized controlled trial of parent-child psychotherapy targeting emotion development for early childhood depression. *Am J Psychiatry*. 2018 Nov 1;175(11):1102-10. doi: 10.1176/appi.ajp.2018.18030321. PMID: 29921144.
- 205. Hoyniak CP, Whalen DJ, Barch D, et al. Sleep problems in preschool-onset major depressive disorder: the effect of treatment with parent—child interaction therapy-emotion development. *Eur Child Adolesc Psychiatry*. 2020doi: 10.1007/s00787-020-01641-1. PMID: CN-02193938.
- 206. Lyneham HJ, Rapee RM. Evaluation of therapist-supported parent-implemented CBT for anxiety disorders in rural children. *Behav Res Ther*. 2006;44(9):1287-300. doi: 10.1016/j.brat.2005.09.009. PMID: 2006-09968-007.
- 207. March J, Silva S, Petrycki S, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA*. 2004 Aug 18;292(7):807-20. doi: 10.1001/jama.292.7.807. PMID: 15315995.
- 208. Curry J, Rohde P, Simons A, et al. Predictors and moderators of acute outcome in the Treatment for Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1427-39. doi: 10.1097/01.chi.0000240838.78984.e2. PMID: 17135988.

- 209. Emslie G, Kratochvil C, Vitiello B, et al. Treatment for Adolescents with Depression Study (TADS): safety results. *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1440-55. doi: 10.1097/01.chi.0000240840.63737.1d. PMID: 17135989.
- 210. Kennard B, Silva S, Vitiello B, et al. Remission and residual symptoms after short-term treatment in the Treatment of Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1404-11. doi: 10.1097/01.chi.0000242228.75516.21. PMID: 17135985.
- 211. Vitiello B, Rohde P, Silva S, et al. Functioning and quality of life in the Treatment for Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1419-26. doi: 10.1097/01.chi.0000242229.52646.6e. PMID: 17135987.
- 212. Mehlum L, Tørmoen AJ, Ramberg M, et al. Dialectical behavior therapy for adolescents with repeated suicidal and self-harming behavior: a randomized trial. *J Am Acad Child Adolesc Psychiatry*. 2014 Oct;53(10):1082-91. doi: 10.1016/j.jaac.2014.07.003. PMID: 25245352.
- 213. Mehlum L, Ramberg M, Tørmoen AJ, et al. Dialectical behavior therapy compared with enhanced usual care for adolescents with repeated suicidal and self-harming behavior: outcomes over a one-year follow-up. *J Am Acad Child Adolesc Psychiatry*. 2016 Apr;55(4):295-300. doi: 10.1016/j.jaac.2016.01.005. PMID: 27015720.
- 214. Mehlum L, Ramleth RK, Tørmoen AJ, et al. Long term effectiveness of dialectical behavior therapy versus enhanced usual care for adolescents with self-harming and suicidal behavior. *J Child Psychol Psychiatry*. 2019 Oct;60(10):1112-22. doi: 10.1111/jcpp.13077. PMID: 31127612.
- 215. Haga E, Aas E, Grøholt B, et al. Cost-effectiveness of dialectical behaviour therapy vs. enhanced usual care in the treatment of adolescents with self-harm. *Child Adolesc Psychiatry Ment Health*. 2018;12:22. doi: 10.1186/s13034-018-0227-2. PMID: 29743941.
- 216. Mufson L, Dorta KP, Wickramaratne P, et al. A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. *Arch Gen Psychiatry*. 2004 Jun;61(6):577-84. doi: 10.1001/archpsyc.61.6.577. PMID: 15184237.
- 217. McGlinchey EL, Reyes-Portillo JA, Turner JB, et al. Innovations in Practice: The relationship betweensleep disturbances, depression, and interpersonal functioning in treatment for adolescent depression. *Child Adolesc Ment Health*. 2017 May;22(2):96-9. doi: 10.1111/camh.12176. PMID: 28947892.
- 218. Muris P, Merckelbach H, Kindt M, et al. The utility of Screen for Child Anxiety Related Emotional Disorders (SCARED) as a tool for identifying children at high risk for prevalent anxiety disorders. *Anxiety, Stress & Coping: An International Journal*. 2001;14(3):265-83. doi: 10.1080/10615800108248357. PMID: 2002-00834-002.
- 219. O'Connor S, Ferguson E, Carney T, et al. The development and evaluation of the paediatric index of emotional distress (PI-ED). *Soc Psychiatry Psychiatr Epidemiol*. 2016 Jan;51(1):15-26. doi: 10.1007/s00127-015-1134-y. PMID: 26687238.
- 220. Öst L-G, Cederlund R, Reuterskiöld L. Behavioral treatment of social phobia in youth: does parent education training improve the outcome? *Behav Res Ther*. 2015;67:19-29. doi: 10.1016/j.brat.2015.02.001. PMID: 2015-12473-003.
- 221. Ougrin D, Boege I, Stahl D, et al. Randomised controlled trial of therapeutic assessment versus usual assessment in adolescents with self-harm: 2-year follow-up. *Arch Dis Child*. 2013 Oct;98(10):772-6. doi: 10.1136/archdischild-2012-303200. PMID: 23709314.

- 222. Ougrin D, Zundel T, Ng A, et al. Trial of therapeutic assessment in London: randomised controlled trial of therapeutic assessment versus standard psychosocial assessment in adolescents presenting with self-harm. *Arch Dis Child*. 2011 Feb;96(2):148-53. doi: 10.1136/adc.2010.188755. PMID: 21030367.
- 223. Patton GC, Coffey C, Posterino M, et al. A computerised screening instrument for adolescent depression: population-based validation and application to a two-phase case-control study. *Soc Psychiatry Psychiatr Epidemiol*. 1999 Mar;34(3):166-72. PMID: 10327843.
- 224. Perrin S, Bevan D, Payne S, et al. GAD-specific cognitive behavioral treatment for children and adolescents: a pilot randomized controlled trial. *Cognit Ther Res.* 2019doi: 10.1007/s10608-019-10020-3. PMID: CN-01941262.
- 225. Pine DS, Walkup JT, Labellarte MJ, et al. Fluvoxamine for the treatment of anxiety disorders in children and adolescents. *N Engl J Med*. 2001;344(17):1279-85. doi: 10.1056/NEJM200104263441703. PMID: CN-00343009.
- 226. Walkup JT, Labellarte MJ, Riddle MA, et al. Searching for moderators and mediators of pharmacological treatment effects in children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2003 Jan;42(1):13-21. doi: 10.1097/00004583-200301000-00006. PMID: 12500072.
- 227. Ginsburg GS, Riddle MA, Davies M. Somatic symptoms in children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2006 Oct;45(10):1179-87. doi: 10.1097/01.chi.0000231974.43966.6e. PMID: 17003663.
- 228. Reinblatt SP, dosReis S, Walkup JT, et al. Activation adverse events induced by the selective serotonin reuptake inhibitor fluvoxamine in children and adolescents. *J Child Adolesc Psychopharmacol*. 2009;19(2):119-26. doi: 10.1089/cap.2008.040. PMID: 2009-05505-003.
- 229. Pineda J, Dadds MR. Family intervention for adolescents with suicidal behavior: a randomized controlled trial and mediation analysis. *J Am Acad Child Adolesc Psychiatry*. 2013 Aug;52(8):851-62. doi: 10.1016/j.jaac.2013.05.015. PMID: 23880495.
- 230. Queen AH, Ehrenreich-May J, Hershorin ER. Preliminary validation of a screening tool for adolescent panic disorder in pediatric primary care clinics. *Child Psychiatry Hum Dev*. 2012 Apr;43(2):171-83. doi: 10.1007/s10578-011-0256-z. PMID: 21938484.
- 231. Ranta K, Kaltiala-Heino R, Rantanen P, et al. Screening social phobia in adolescents from general population: the validity of the Social Phobia Inventory (SPIN) against a clinical interview. *Eur Psychiatry*. 2007 May;22(4):244-51. doi: 10.1016/j.eurpsy.2006.12.002. PMID: 17346941.
- 232. Ranta K, Kaltiala-Heino R, Rantanen P, et al. The Mini-Social Phobia Inventory: psychometric properties in an adolescent general population sample. *Compr Psychiatry*. 2012 Jul;53(5):630-7. doi: 10.1016/j.comppsych.2011.07.007. PMID: 21944882.
- 233. Richardson LP, Ludman E, McCauley E, et al. Collaborative care for adolescents with depression in primary care: a randomized clinical trial. *JAMA*. 2014 Aug 27;312(8):809-16. doi: 10.1001/jama.2014.9259. PMID: 25157724.
- 234. Rivera-Riquelme M, Piqueras JA, Cuijpers P. The Revised Mental Health Inventory-5 (MHI-5) as an ultra-brief screening measure of bidimensional mental health in children and adolescents. *Psychiatry Res.* 2019 Apr;274:247-53. doi: 10.1016/j.psychres.2019.02.045. PMID: 30818147.

- 235. Roberts RE, Lewinsohn PM, Seeley JR. Screening for adolescent depression: a comparison of depression scales. *J Am Acad Child Adolesc Psychiatry*. 1991 Jan;30(1):58-66. doi: 10.1097/00004583-199101000-00009. PMID: 2005065.
- 236. Rossouw TI, Fonagy P. Mentalization-based treatment for self-harm in adolescents: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2012 Dec;51(12):1304-13.e3. doi: 10.1016/j.jaac.2012.09.018. PMID: 23200287.
- 237. Rudy BM, Zavrou S, Johnco C, et al. Parent-led exposure therapy: a pilot study of a brief behavioral treatment for anxiety in young children. *J Child Fam Stud*. 2017;26(9):2475-84. doi: 10.1007/s10826-017-0772-y. PMID: 2017-22955-001.
- 238. Rynn MA, Siqueland L, Rickels K. Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. *Am J Psychiatry*. 2001 Dec;158(12):2008-14. doi: 10.1176/appi.ajp.158.12.2008. PMID: 11729017.
- 239. Salzer S, Stefini A, Kronmüller KT, et al. Cognitive-behavioral and psychodynamic therapy in adolescents with social anxiety disorder: a multicenter randomized controlled trial. *Psychother Psychosom*. 2018;87(4):223-33. doi: 10.1159/000488990. PMID: 29895001.
- 240. Sánchez-García R, Olivares Rodríguez J. Effectiveness of a program for early detection/intervention in children/adolescents with generalized social phobia. *Anales de Psicología*. 2009.
- 241. Shortt AL, Barrett PM, Fox TL. Evaluating the FRIENDS program: a cognitive-behavioral group treatment for anxious children and their parents. *J Clin Child Psychol*. 2001 Dec;30(4):525-35. doi: 10.1207/s15374424jccp3004_09. PMID: 11708240.
- 242. Stjerneklar S, Hougaard E, McLellan LF, et al. A randomized controlled trial examining the efficacy of an internet-based cognitive behavioral therapy program for adolescents with anxiety disorders. *PLoS One*. 2019;14(9):e0222485. doi: 10.1371/journal.pone.0222485. PMID: 31532802.
- 243. Strawn JR, Prakash A, Zhang Q, et al. A randomized, placebo-controlled study of duloxetine for the treatment of children and adolescents with generalized anxiety disorder. *J Am Acad Child Adolesc Psychiatry*. 2015 Apr;54(4):283-93. doi: 10.1016/j.jaac.2015.01.008. PMID: 25791145.
- 244. Strawn JR, Mills JA, Schroeder H, et al. Escitalopram in adolescents with generalized anxiety disorder: a double-blind, randomized, placebo-controlled study. *J Clin Psychiatry*. 2020 Aug 25;81(5)doi: 10.4088/JCP.20m13396. PMID: 32857933.
- 245. Tang TC, Jou SH, Ko CH, et al. Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and parasuicide behaviors. *Psychiatry Clin Neurosci*. 2009 Aug;63(4):463-70. doi: 10.1111/j.1440-1819.2009.01991.x. PMID: 19531111.
- 246. Thirlwall K, Cooper PJ, Karalus J, et al. Treatment of child anxiety disorders via guided parent-delivered cognitive-behavioural therapy: randomised controlled trial. *Br J Psychiatry*. 2013;203(6):436-44. doi: 10.1192/bjp.bp.113.126698. PMID: CN-00910881.
- 247. Thompson EA, Eggert LL. Using the suicide risk screen to identify suicidal adolescents among potential high school dropouts. *J Am Acad Child Adolesc Psychiatry*. 1999 Dec;38(12):1506-14. doi: 10.1097/00004583-199912000-00011. PMID: 10596250.
- 248. Topooco N, Berg M, Johansson S, et al. Chat- and internet-based cognitive-behavioural therapy in treatment of adolescent depression: randomised controlled trial. *BJPsych Open*. 2018 Jul;4(4):199-207. doi: 10.1192/bjo.2018.18. PMID: 29988969.

- 249. Topooco N, Byléhn S, Dahlström Nysäter E, et al. Evaluating the efficacy of internet-delivered cognitive behavioral therapy blended with synchronous chat sessions to treat adolescent depression: randomized controlled trial. *J Med Internet Res.* 2019 Nov 1;21(11):e13393. doi: 10.2196/13393. PMID: 31682572.
- 250. Tsai CF, Wang SJ, Juang KD, et al. Use of the Chinese (Taiwan) version of the Social Phobia Inventory (SPIN) among early adolescents in rural areas: reliability and validity study. *J Chin Med Assoc*. 2009 Aug;72(8):422-9. doi: 10.1016/s1726-4901(09)70399-5. PMID: 19686998.
- 251. Villabø MA, Narayanan M, Compton SN, et al. Cognitive—behavioral therapy for youth anxiety: an effectiveness evaluation in community practice. *J Consult Clin Psychol*. 2018;86(9):751-64. doi: 10.1037/ccp0000326. PMID: 2018-41322-004.
- 252. Wagner KD, Jonas J, Findling RL, et al. A double-blind, randomized, placebo-controlled trial of escitalopram in the treatment of pediatric depression. *J Am Acad Child Adolesc Psychiatry*. 2006 Mar;45(3):280-8. doi: 10.1097/01.chi.0000192250.38400.9e. PMID: 16540812.
- 253. Waite P, Marshall T, Creswell C. A randomized controlled trial of internet-delivered cognitive behaviour therapy for adolescent anxiety disorders in a routine clinical care setting with and without parent sessions. *Child Adolesc Ment Health*. 2019. doi: 10.1111/camh.12311. PMID: CN-01917999.
- 254. Walkup JT, Albano AM, Piacentini J, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *N Engl J Med*. 2008 Dec 25;359(26):2753-66. doi: 10.1056/NEJMoa0804633. PMID: 18974308.
- 255. Albano AM, Comer JS, Compton SN, et al. Secondary outcomes from the child/adolescent anxiety multimodal study: implications for clinical practice. *Evid Based Pract Child Adolesc Ment Health*. 2018;3(1):30-41. doi: 10.1080/23794925.2017.1399485. PMID: 30906874.
- 256. Taylor JH, Lebowitz ER, Jakubovski E, et al. Monotherapy insufficient in severe anxiety? Predictors and moderators in the child/adolescent anxiety multimodal study. *J Clin Child Adolesc Psychol*. 2018 Mar-Apr;47(2):266-81. doi: 10.1080/15374416.2017.1371028. PMID: 28956620.
- 257. Compton SN, Peris TS, Almirall D, et al. Predictors and moderators of treatment response in childhood anxiety disorders: results from the CAMS trial. *J Consult Clin Psychol*. 2014 Apr;82(2):212-24. doi: 10.1037/a0035458. PMID: 24417601.
- 258. Caporino NE, Read KL, Shiffrin N, et al. Sleep-related problems and the effects of anxiety treatment in children and adolescents. *J Clin Child Adolesc Psychol*. 2017 Sep-Oct;46(5):675-85. doi: 10.1080/15374416.2015.1063429. PMID: 26467211.
- 259. Sanchez AL, Comer JS, Coxe S, et al. The effects of youth anxiety treatment on school impairment: differential outcomes across CBT, sertraline, and their combination. *Child Psychiatry Hum Dev*. 2019 Dec;50(6):940-9. doi: 10.1007/s10578-019-00896-3. PMID: 31087216.
- 260. Rynn MA, Walkup JT, Compton SN, et al. Child/adolescent anxiety multimodal study: evaluating safety. *J Am Acad Child Adolesc Psychiatry*. 2015 Mar;54(3):180-90. doi: 10.1016/j.jaac.2014.12.015. PMID: 25721183.
- 261. Gordon-Hollingsworth AT, Becker EM, Ginsburg GS, et al. Anxiety disorders in Caucasian and African American children: a comparison of clinical characteristics,

- treatment process variables, and treatment outcomes. *Child Psychiatry Hum Dev*. 2015;46(5):643-55. doi: 10.1007/s10578-014-0507-x. PMID: 2014-43106-001.
- 262. Ginsburg GS, Kendall PC, Sakolsky D, et al. Remission after acute treatment in children and adolescents with anxiety disorders: findings from the CAMS. *J Consult Clin Psychol*. 2011 Dec;79(6):806-13. doi: 10.1037/a0025933. PMID: 22122292.
- 263. Weersing VR, Brent DA, Rozenman MS, et al. Brief behavioral therapy for pediatric anxiety and depression in primary care: a randomized clinical trial. *JAMA Psychiatry*. 2017 Jun 1;74(6):571-8. doi: 10.1001/jamapsychiatry.2017.0429. PMID: 28423145.
- 264. Brent DA, Porta G, Rozenman MS, et al. Brief behavioral therapy for pediatric anxiety and depression in primary care: a follow-up. *J Am Acad Child Adolesc Psychiatry*. 2019 Jul 3doi: 10.1016/j.jaac.2019.06.009. PMID: 31278996.
- 265. Wood A, Trainor G, Rothwell J, et al. Randomized trial of group therapy for repeated deliberate self-harm in adolescents. *J Am Acad Child Adolesc Psychiatry*. 2001 Nov;40(11):1246-53. doi: 10.1097/00004583-200111000-00003. PMID: 11699797.
- 266. Lindqvist K, Mechler J, Carlbring P, et al. Affect-focused psychodynamic internet-based therapy for adolescent depression: randomized controlled trial. *J Med Internet Res*. 2020;22(3):e18047. doi: 10.2196/18047. PMID: CN-02099453.
- 267. Gould MS, Marrocco FA, Kleinman M, et al. Evaluating iatrogenic risk of youth suicide screening programs: a randomized controlled trial. *JAMA*. 2005 Apr 6;293(13):1635-43. doi: 10.1001/jama.293.13.1635. PMID: 15811983.
- 268. Robinson J, Pan Yuen H, Martin C, et al. Does screening high school students for psychological distress, deliberate self-harm, or suicidal ideation cause distress--and is it acceptable? An Australian-based study. *Crisis*. 2011;32(5):254-63. doi: 10.1027/0227-5910/a000087. PMID: 21940259.
- 269. Muris P, Steerneman P. The revised version of the Screen for Child Anxiety Related Emotional Disorders (SCARED–R): first evidence for its reliability and validity in a clinical sample. *Br J Clin Psychol*. 2001;40(1):35-44. doi: 10.1348/014466501163463. PMID: 2001-06105-003.
- 270. O'Connor E, Senger CA, Henninger M, et al. US Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Interventions to Prevent Perinatal Depression: A Systematic Evidence Review for the US Preventive Services Task Force. Agency for Healthcare Research and Ouality; 2019.
- 271. Mammarella IC, Donolato E, Caviola S, et al. Anxiety profiles and protective factors: a latent profile analysis in children. *Pers Individ Dif.* 2018;124:201-8. doi: 10.1016/j.paid.2017.12.017. PMID: 2018-01016-035.
- 272. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961 Jun;4:561-71. doi: 10.1001/archpsyc.1961.01710120031004. PMID: 13688369.
- 273. Radloff LS. The CES-D Scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1(3):385–401. doi: 10.1177/014662167700100306.
- 274. Fillenbaum GG, Burchett BM, Blazer DG. Identifying a National Death Index match. *Am J Epidemiol*. 2009 Aug 15;170(4):515-8. doi: 10.1093/aje/kwp155. PMID: 19567777.
- 275. Osimo EF, Stochl J, Zammit S, et al. Longitudinal population subgroups of CRP and risk of depression in the ALSPAC birth cohort. *Compr Psychiatry*. 2020;96doi: 10.1016/j.comppsych.2019.152143. PMID: 2020-00258-001.

- 276. van Gastel W, Ferdinand RF. Screening capacity of the Multidimensional Anxiety Scale for Children (MASC) for DSM-IV anxiety disorders. *Depress Anxiety*. 2008;25(12):1046-52. doi: 10.1002/da.20452. PMID: 18833579.
- 277. Wagner KD, Robb AS, Findling RL, et al. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. *Am J Psychiatry*. 2004 Jun;161(6):1079-83. doi: 10.1176/appi.ajp.161.6.1079. PMID: 15169696.
- 278. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. *J Consult Clin Psychol*. 1991;59(1):12-9. doi: 10.1037/0022-006x.59.1.12.
- 279. Johnco CJ, Salloum A, Lewin AB, et al. Refining clinical judgment of treatment response and symptom remission identification in childhood anxiety using a signal detection analysis on the Pediatric Anxiety Rating Scale. *J Child Adolesc Psychopharmacol*. 2015 Nov;25(9):674-83. doi: 10.1089/cap.2015.0102. PMID: 26579629.
- 280. Vitiello B, Silva SG, Rohde P, et al. Suicidal events in the Treatment for Adolescents With Depression Study (TADS). *J Clin Psychiatry*. 2009 Apr 21;70(5):741-7. doi: 10.4088/jcp.08m04607. PMID: 19552869.
- 281. Horowitz LM, Bridge JA, Teach SJ, et al. Ask Suicide-Screening Questions (ASQ): a brief instrument for the pediatric emergency department. *Arch Pediatr Adolesc Med*. 2012 Dec;166(12):1170-6. doi: 10.1001/archpediatrics.2012.1276. PMID: 23027429.
- 282. Aguinaldo LD, Sullivant S, Lanzillo EC, et al. Validation of the ask suicide-screening questions (ASQ) with youth in outpatient specialty and primary care clinics. *Gen Hosp Psychiatry*. 2021 Jan-Feb;68:52-8. doi: 10.1016/j.genhosppsych.2020.11.006. PMID: 33310014.
- 283. The Joint Commission. Suicide prevention. 2021. https://www.jointcommission.org/resources/patient-safety-topics/suicide-prevention/.
- 284. National Institutes of Health. Ask Suicide-Screening Questions (ASQ) toolkit. no date. https://www.nimh.nih.gov/research/research-conducted-at-nimh/asq-toolkit-materials.
- 285. Rinke ML, Bundy DG, Stein REK, et al. Increasing recognition and diagnosis of adolescent depression: Project RedDE: a cluster randomized trial. *Pediatr Qual Saf.* 2019 Sep-Oct;4(5):e217. doi: 10.1097/pq9.000000000000217. PMID: 31745520.
- 286. eCQI. Preventive care and screening: screening for depression and follow-up plan. eCQI; n.d. https://ecqi.healthit.gov/ecqm/ep/2019/cms002v8. Accessed April 30, 2021.
- 287. Quality Payment Program. MIPS explore measures & activities. Baltimore, MD: Centers for Medicare & Medicaid Services; n.d. https://qpp.cms.gov/mips/explore-measures?tab=qualityMeasures&py=2021. Accessed April 30, 2021.
- 288. NCQA. HEDIS depression measures for electronic clinical data. NCQA; n.d. https://www.ncqa.org/hedis/the-future-of-hedis/hedis-depression-measures-for-electronic-clinical-data/. Accessed April 30, 2021.
- 289. Pfizer. Patient health questionnaire (PHQ) screeners. Pfizer; n.d. https://www.phqscreeners.com/select-screener. Accessed April 30, 2021.
- 290. Aboustate N, Raven M, Klau J, et al. 28 reanalysis of the treatment for adolescents with depression study (TADS) under the restoring invisible and abandoned trials initiative (RIAT). *BMJ Evidence-Based Medicine*. 2019;24:A20-A1. doi: 10.1136/bmjebm-2019-POD.42.

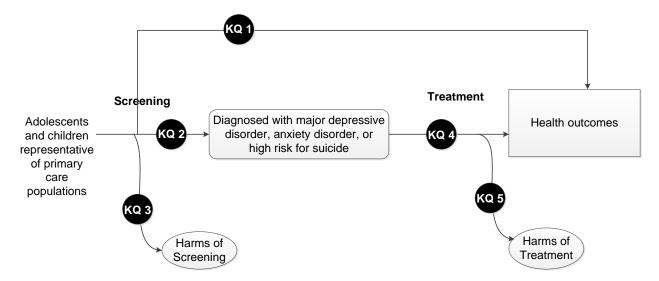
- 291. Doshi P, Dickersin K, Healy D, et al. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ*. 2013 Jun 13;346:f2865. doi: 10.1136/bmj.f2865. PMID: 23766480.
- 292. U.S. Food and Drug Administration. Suicidality in children and adolescents being treated with antidepressant medications. Silver Spring, MD: Food and Drug Administration; 2018. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/suicidality-children-and-adolescents-being-treated-antidepressant-medications. Accessed February 15, 2021.
- 293. Hammad TA, Laughren T, Racoosin J. Suicidality in pediatric patients treated with antidepressant drugs. *Arch Gen Psychiatry*. 2006 Mar;63(3):332-9. doi: 10.1001/archpsyc.63.3.332. PMID: 16520440.
- 294. Paauw C, de Roos C, Tummers J, et al. Effectiveness of trauma-focused treatment for adolescents with major depressive disorder. *Eur J Psychotraumatol*. 2019;10(1):1682931. doi: 10.1080/20008198.2019.1682931. PMID: 31762948.
- 295. McCrory E, De Brito SA, Viding E. The link between child abuse and psychopathology: a review of neurobiological and genetic research. *J R Soc Med*. 2012 Apr;105(4):151-6. doi: 10.1258/jrsm.2011.110222. PMID: 22532655.
- 296. Horowitz LM, Mournet AM, Lanzillo E, et al. Screening pediatric medical patients for suicide risk: is depression screening enough? *J Adolesc Health*. 2021 Jun;68(6):1183-8. doi: 10.1016/j.jadohealth.2021.01.028. PMID: 33712380.
- 297. Mournet AM, Bridge JA, Ross A, et al. A comparison of suicide attempt histories of pediatric and adult medical inpatients and implications for screening. *Arch Suicide Res*. 2021 Jun 8:1-15. doi: 10.1080/13811118.2021.1931596. PMID: 34101537.
- 298. Ford I, Norrie J. Pragmatic trials. *N Engl J Med*. 2016;375(5):454-63. doi: 10.1056/NEJMra1510059. PMID: 27518663.
- 299. Asarnow JR, Jaycox LH, Duan N, et al. Effectiveness of a quality improvement intervention for adolescent depression in primary care clinics: a randomized controlled trial. *JAMA*. 2005 Jan 19;293(3):311-9. doi: 10.1001/jama.293.3.311. PMID: 15657324.
- 300. Asarnow JR, Jaycox LH, Tang L, et al. Long-term benefits of short-term quality improvement interventions for depressed youths in primary care. *Am J Psychiatry*. 2009 Sep;166(9):1002-10. doi: 10.1176/appi.ajp.2009.08121909. PMID: 19651711.
- 301. McCauley E, Berk MS, Asarnow JR, et al. Efficacy of dialectical behavior therapy for adolescents at high risk for suicide: a randomized clinical trial. *JAMA Psychiatry*. 2018 Aug 1;75(8):777-85. doi: 10.1001/jamapsychiatry.2018.1109. PMID: 29926087.
- 302. Miller IW, Camargo CA, Jr., Arias SA, et al. Suicide prevention in an emergency department population: the ED-SAFE Study. *JAMA Psychiatry*. 2017 Jun 1;74(6):563-70. doi: 10.1001/jamapsychiatry.2017.0678. PMID: 28456130.
- 303. National Institute for Health and Care Excellence. Depression in children and young people: identifification and management. NICE guideline [NG134]. United Kingdom: National Institute for Health and Care Excellence; 2019.

 https://www.nice.org.uk/guidance/ng134/chapter/Recommendations. Accessed August 12, 2019.
- 304. Kliem S, Lohmann A, Mößle T, et al. Psychometric properties and measurement invariance of the Beck hopelessness scale (BHS): results from a German representative population sample. *BMC Psychiatry*. 2018 Apr 25;18(1):110. doi: 10.1186/s12888-018-1646-6. PMID: 29699522.

- 305. King CA, Hill RM, Wynne HA, et al. Adolescent suicide risk screening: the effect of communication about type of follow-up on adolescents' screening responses. *J Clin Child Adolesc Psychol*. 2012;41(4):508-15. doi: 10.1080/15374416.2012.680188. PMID: 22540534.
- 306. Erford BT, Jackson J, Bardhoshi G, et al. Selecting suicide ideation assessment instruments: a meta-analytic review. *Measurement and Evaluation in Counseling and Development*. 2017;51(1):42-59. doi: 10.1080/07481756.2017.1358062.
- 307. Reynolds WM, Mazza JJ. Assessment of suicidal ideation in inner-city children and young adolescents: reliability and validity of the suicidal ideation questionnaire-JR. *School Psych Rev.* 1999;28(1):17-30.
- 308. Gowers SG, Harrington RC, Whitton A, et al. Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA). Glossary for HoNOSCA score sheet. *Br J Psychiatry*. 1999 May;174:428-31. doi: 10.1192/bjp.174.5.428. PMID: 10616610.
- 309. NSW Department of Health MH-Oat Project. Childrens Global Assessment Scale (CGAS). St. Leonards, Australia: NSW Department of Health; 2002. https://www.thereachinstitute.org/images/CGAS.pdf. Accessed April 19, 2021.
- 310. Silverman WK, Albano AM. The anxiety disorders interview schedule for children for DSM-IV: clinician manual (child and parent versions). San Antonio, TX: The Psychological Corporation; 1996.
- 311. Carruthers S, Kent R, Hollocks MJ, et al. Brief report: testing the psychometric properties of the Spence Children's Anxiety Scale (SCAS) and the Screen for Child Anxiety Related Emotional Disorders (SCARED) in Autism Spectrum Disorder. *J Autism Dev Disord*. 2020 Jul;50(7):2625-32. doi: 10.1007/s10803-018-3774-8. PMID: 30334126.
- 312. Bunnell BE, Beidel DC, Liu L, et al. The SPAIC-11 and SPAICP-11: two brief child- and parent-rated measures of social anxiety. *J Anxiety Disord*. 2015 Dec;36:103-9. doi: 10.1016/j.janxdis.2015.10.002. PMID: 26500188.
- 313. Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)*. 2007 Jul;4(7):28-37. PMID: 20526405.
- 314. Gilroy S. The Revised Children's Manifest Anxiety Scale (RCMAS). "What I think and feel". n.d. http://www.clintools.com/victims/resources/assessment/affect/rcmas.html. Accessed April 19, 2021.
- 315. The pediatric anxiety rating scale (PARS): development and psychometric properties. *J Am Acad Child Adolesc Psychiatry*. 2002 Sep;41(9):1061-9. doi: 10.1097/00004583-200209000-00006. PMID: 12218427.
- 316. Ginsburg GS, Keeton CP, Drazdowski TK, et al. The utility of clinicians ratings of anxiety using the Pediatric Anxiety Rating Scale (PARS). *Child & Youth Care Forum*. 2011;40(2):93-105. doi: 10.1007/s10566-010-9125-3. PMID: 2011-06151-001.
- 317. Sparse whole-genome sequencing identifies two loci for major depressive disorder. *Nature*. 2015 Jul 30;523(7562):588-91. doi: 10.1038/nature14659. PMID: 26176920.
- 318. Langley AK, Falk A, Peris T, et al. The child anxiety impact scale: examining parent-and child-reported impairment in child anxiety disorders. *J Clin Child Adolesc Psychol*. 2014;43(4):579-91. doi: 10.1080/15374416.2013.817311. PMID: 23915200.
- 319. Evans R, Thirlwall K, Cooper P, et al. Using symptom and interference questionnaires to identify recovery among children with anxiety disorders. *Psychol Assess*. 2017 Jul;29(7):835-43. doi: 10.1037/pas0000375. PMID: 27845527.

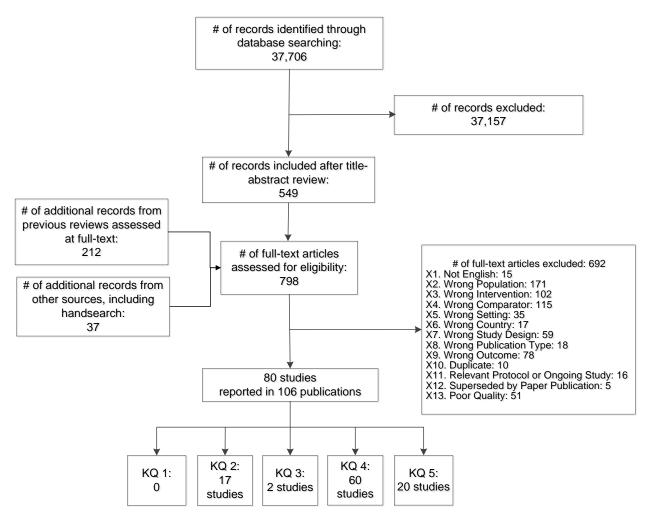
- 320. Psychiatry & Behavioral Health Learning Network. Beck Depression Inventory-II (BDI-II). Psychiatry & Behavioral Health Learning Network; 1996. https://www.psychcongress.com/saundras-corner/scales-screenersdepression/beck-depression-inventory-ii-bdi-ii. Accessed April 26, 2021.
- 321. Mayes TL, Bernstein IH, Haley CL, et al. Psychometric properties of the Children's Depression Rating Scale-Revised in adolescents. *J Child Adolesc Psychopharmacol*. 2010 Dec;20(6):513-6. doi: 10.1089/cap.2010.0063. PMID: 21186970.

Figure 1. Analytic Framework



Abbreviation: KQ=key question.

Figure 2. Flow Diagram of Studies



Abbreviations: KQ=key question; X=exclusion number.

Table 1. Non-USPSTF Guidelines and Recommendations on Screening for Anxiety, Depression, and Suicide Risk for Children and Adolescents

Organization	Recommendation					
o. gamzadon	Suicide Risk					
The American Academy of Child and Adolescent Psychiatry, 2019 ¹⁴³	Recommends screening for suicide risk across physical and mental healthcare settings and the urgent identification of and clinical intervention for children and youth at risk for suicide.					
American Academy of Pediatrics, Bright Futures, 2022 ¹⁴²	Recommends universal screening for youth 12 years or older and screening when clinically indicated for youth 8 to 11 years. For youth under age 8, screening is not indicated but pediatricians should assess for suicidal thought and behaviors if warning signs of suicide risk or parent report of suicidal behaviors are present.					
American Academy of Family Physicians, 2017 ¹⁴¹	Supports the USPSTF recommendation.					
The Joint Commission National Patient Safety Goal for Suicide Prevention, 2019 ¹⁴⁴	Organizations should screen all individuals served for suicidal ideation using a validated screening tool and monitor implementation and effectiveness of policies and procedures for screening individuals at risk for suicide and take actions to improve compliance as needed.					
	Anxiety					
American Academy of Child and Adolescent Psychiatry (AACAP), 2020 ¹⁴⁵	Notes the lack of empirical recommendations on screening for anxiety disorders in children or adolescents and points to freely available screening instruments.					
National Institute for Health and Clinical Excellence (NICE), 2017 ¹⁴⁶	Recommends asking children or young people about their feelings of anxiety, fear, avoidance, or distress and conducting comprehensive assessments of those reporting those feelings.					
	Depression					
Guidelines for Adolescent Depression in Primary Care (GLAD-PC), 2018 ¹⁴⁷	Recommends annual universal depression screening of youth 12 years or older with a formal screening tool, identification of patients at high risk for depression, coordination of depression care, and establishment of a safety plan.					
National Institute for Health and Clinical Excellence (NICE), 2019 ³⁰³	Notes that healthcare professionals in primary care settings should be familiar with screening for mood disorders. Healthcare professionals in primary care, schools, and other relevant community settings should be trained to detect symptoms of depression and assess children and young people who may be at risk of depression. Training should include the evaluation of recent and past psychosocial risk factors.					
American Academy of Family Physicians, 2017 ¹⁴¹	Supports the USPSTF recommendation.					
	Multicondition					
American Academy of Pediatrics (AAP), Bright Futures, 2015 ¹⁵⁰	Recommends screening annually for emotional and behavioral problems for adolescent patients ages 12 years or older.					
American College of Obstetricians and Gynecologists, 2017 (reaffirmed in 2020) ¹⁵¹	During preventive care visits, all adolescents should be screened for any mental health disorder in a confidential setting (if allowed by the laws of that locality).					

Abbreviations: AACAP=American Academy of Child and Adolescent Psychiatry; AAP=American Academy of Pediatrics; AMA=American Medical Association; GLAD-PC=Guidelines for Adolescent Depression in Primary Care; NICE=National Institute for Health and Clinical Excellence; USPSTF=U.S. Preventive Services Task Force.

Table 2. Results of Diagnostic Test Accuracy Studies on Screening for Anxiety Compared With Structured Clinical Interview (KQ 2)

								Per 1,000 Screens Across a Prevalence From 3% to 13%	Per 1,000 Screens Across a Prevalence From 3% to 13%
Author, Year	Age Range; Mean Age	Total N	Index Test		Prevalence	Sensitivity	Specificity	No. False-	No. False-
Quality	(SD), Years	(% Female)	Cutoff	Respondent	%	(95% CI)	(95% CI)	Negatives	Positives
			Anxiety (Global, tha	t is positive o	n total anxiet	y score)			
Screen for Anxiety Rel	ated Emotiona	l Disorders (S							
Canals et al, 2012 ¹⁷¹ Fair	11 (1.0) 9 to 13	562 (55)	SCARED-C Cutoff > 25	Youth	24	0.76 (0.68 to 0.92)	0.68 (0.63 to 0.72)	6 to 31	278 to 312
			SCARED-P Cutoff > 17	Parents	24	0.63 (0.54 to 0.74)	0.70 (0.65 to 0.74)	9 to 48	261 to 293
			SCARED-C Short Cutoff ≥ 3	Youth	24	0.67 (0.59 to 0.74)	0.74 (0.70 to 0.78)	8 to 43	226 to 254
			SCARED-P Short Cutoff > 3	Parents	24	0.34 (0.26 to 0.42)	0.86 (0.82 to 0.89)	17 to 86	122 to 137
				GAD					
			Patient Health Que	estionnaire— <i>F</i>	Adolescent (F	PHQ-A)			
Johnson et al, 2002 ¹⁹⁹ Fair	16 (1.2) 13 to 18	403 (63)	PHQ-A Cutoff NR	Youth	2.5	0.50 (0.24 to 0.76)	0.98 (0.86 to 0.99)	13 to 65	17 to 20
SCARED—GAD Scale		` '				,	,		
Muris et al, 2001 ²¹⁸ Fair	10 (1.4) 7 to 14	82 (61)	SCARED-C Male cutoff ≥ 10 Female cutoff ≥ 13	Youth	13	0.64 (0.35 to 0.85)	0.63 (0.52 to 0.74)	9 to 47	322 to 361
Paediatric Index of	f Emotional Dis	stress (PI-ED)-	-Anxiety Scale						
O'Connor et al, 2016 ²¹⁹ Fair	12 (2.5) 8 to 17	100 (48)	PI-ED Cutoff ≥ 9	Youth	6	0.88 (0.53 to 98)	0.85 (0.78 to 0.90)	3 to 16	130 to 146
				Panic Disorde	er				
			Autonomic Nervo	ous System Qu	uestionnaire ((ANS)			
Queen et al, 2012 ²³⁰ Fair	14 (1.8) 12 to 17	45 (43)	ANS 2 questions (cutoff > 1)	Youth	NR	1.00 (NR)	0.47 (NR)	0 to 0	461 to 517
		. ,	ANS 3 questions (cutoff > 2)	Youth	NR	1.00 (NR)	0.57 (NR)	0 to 0	374 to 419
			ANS 5 questions (cutoff \geq 3)	Youth	NR	1.00 (NR)	0.65 (NR)	0 to 0	304 to 341
			Patient Health Que		Adolescent (P				
Johnson et al, 2002 ¹⁹⁹ Fair	16 (1.2) 13 to 18	403 (63)	PHQ – A Cutoff NR	Youth	3	0.42 (0.19 to 0.68)	0.99 (0.97 to 1.0)	15 to 75	9 to 10

Table 2. Results of Diagnostic Test Accuracy Studies on Screening for Anxiety Compared With Structured Clinical Interview (KQ 2)

	Age Range;							Per 1,000 Screens Across a Prevalence From 3% to 13%	Per 1,000 Screens Across a Prevalence From 3% to 13%
Author, Year Quality	Mean Age (SD), Years	Total N (% Female)	Index Test Cutoff	Respondent	Prevalence %	Sensitivity (95% CI)	Specificity (95% CI)	No. False- Negatives	No. False- Positives
				ation Anxiety I					
Screen for Anxiety R									
Muris et al, 2001 ²¹⁸ Fair	10 (1.4) 7 to 14	82 (61)	SCARED-C Male cutoff ≥ 10 Female cutoff ≥ 12		10	0.88 (0.52 to 0.98)	0.73 (0.62 to 0.82)	3 to 16	235 to 263
				ial Anxiety Dis	order				
Screen for Anxiety R				nobia Scale					
Bailey et al, 2006 ¹⁶⁶ Fair	Children Mean: NR	101	SCARED-SP cutoff <u>></u> 5	Parents	9	0.78 (0.45 to 0.94)	0.69 (0.59 to 0.78)	6 to 29	226 to 254
	8 to 12 Adolescents 14 (1.3) 13 to 16	89 (49)*	SCARED-SP Cutoff <u>></u> 6	Parents	13	0.83 (0.55 to 0.95)	0.81 (0. 71 to 0.88)	4 to 22	165 to 185
Social Anxiety Scale	(SAS) Children/	Adolescents							
Bailey et al, 2006 ¹⁶⁶ Fair	Children Mean: NR 8 to 12	101	SAS-C Cutoff <u>></u> 45	Parents	9	0.78 (0.45 to 0.94)	0.74 (0.65 to 0.82)	6 to 29	148 to 166
	Adolescents 14 (1.3 13 to 17	89 (49)*	SAS-A Cutoff <u>></u> 47	Parents	13	0.75 (0.47 to 0.91)	0.80 (0.69 to 0.87)	6 to 32	174 to 195
Garcia-Lopez et al, 2015 ¹⁸⁸ Fair	15 (1.3) 12 to 18	1,034 (54)	SAS-A Cutoff <u>></u> 48	Youth	41	0.93 (0.91 to 0.96)	0.78 (0.74 to 81)	2 to 9	189 to 215
Social Anxiety Scale	for Adolescents	(SASA)							
Garcia-Lopez et al, 2015 ¹⁸⁸ Fair	15 (1.3) 12 to 18	1,034 54	SASA Cutoff <u>></u> 73	Youth	41	0.93 (0.85 to 0.98)	0.79 (0.70 to 87)	2 to 9	183 to 205
Social Phobia and A	nxiety Inventory-	Brief (SPAI-B)							
Garcia-Lopez et al, 2015 ¹⁸⁸ Fair	15 (1.3) 12 to 18	1034 (54)	SPAI-B Cutoff <u>≥</u> 26.4	Youth	41	0.86 (0.83 to 0.89)	0.88 (0.85 to 0.91)	4 to 18	104 to 117
Social Phobia Invent	orv (SPIN)/Mini S	Social Phobia I	nventory (Mini-SPI	N)					
Ranta et al, 2007 ²³¹ Fair	14.7 (1.1) 12 to 17	350 (49)	SPIN Cutoff ≥ 24	Youth	6	0.82 (0.61 to 0.93)	0.85 (0.81 to 0.89)	5 to 23	130 to 146

Table 2. Results of Diagnostic Test Accuracy Studies on Screening for Anxiety Compared With Structured Clinical Interview (KQ 2)

								Per 1,000 Screens Across a Prevalence From 3% to 13%	Per 1,000 Screens Across a Prevalence From 3% to 13%
Author, Year Quality	Age Range; Mean Age (SD), Years	Total N (% Female)	Index Test Cutoff	Respondent	Prevalence %	Sensitivity (95% CI)	Specificity (95% CI)	No. False- Negatives	No. False- Positives
Tsai et al, 2009 ²⁵⁰ Fair	Mean NR 13 to 15	144 (50)	SPIN Cutoff <u>></u> 25	Yourh	10	0.80 (0.55 to 0.93)	0.77 (0.69 to 0.83)	5 to 26	200 to 224
Ranta et al, 2012 ²³² Fair	14.7 (1.1) 12 to 17	350 (49)	Mini-SPIN Cutoff <u>></u> 6	Youth	6	0.86 (0.67 to 0.92)	0.84 (0.79 to 0.87)	4 to 18	139 to 156
Social Worries Questio	nnaire (SWQ)					<u> </u>	· ·		
Bailey et al, 2006 ¹⁶⁶	Children Mean NR	101	SWQ Cutoff > 10	Parents	9	0.67 (0.35 to 0.88)	0.94 (0.88 to 0.98)	8 to 43	52 to 58
	8 to 12 Adolescents 14 (1.3) 13 to 17	89 (49)*	SWQ Cutoff ≥ 5.3	Parents	13	0.83 (0.55 to 0.95)	0.84 (0.74 to 0.90)	4 to 22	139 to 156
			Anxiety Disorde	r (at least one s	pecific anxiety	y disorder)			
Screen for Anxiety Re	lated Emotiona	l Disorders (P	HQ-A)	·					
Johnson et al, 2002 ¹⁹⁹ Fair	16 (1.2) 13 to 18	403 (63)	PHQ-A Cutoff NR	Youth	5	0.50 (0.30 to 0.70)	0.98 (0.96 to 0.99)	12 to 65	17 to 20
Screen for Anxiety Remarks Muris et al, 2001 ²¹⁸	10 (1.4)	82	SCARED-C	Youth	20	0.88	0.56	3 to 16	383 to 429
Fair	7 to 14	62 (61)	NA	TOULIT	20	(0.63 to 0.96)		3 10 10	303 10 429

^{*} Percentage of females in Bailey is for entire sample.

Abbreviations: ANS=Autonomic Nervous System Questionnaire; CI=confidence interval; GAD=general anxiety disorder; KQ=key question; NA=not applicable; NR=not reported; PHQ-A=Patient Health Questionnaire—Adolescent; PI-ED=pediatric index of emotional distress; SAS=social anxiety scale; SAS-A (SASA)=social anxiety scale; adolescents; SASC=social anxiety scale for children; SCARED=Screen for Anxiety Related Emotional Disorders; SCARED-C=Screen for Anxiety Related Emotional Disorders Child version; SCARED-P=Screen for Anxiety Related Emotional Disorders-Social Phobia Scale; SD=standard deviation; SPAI-B=social phobia and anxiety inventory-brief; SPIN=Social Phobia Inventory; SWQ=social worries questionnaire.

Table 3. Characteristics and Results of Test Accuracy Studies for Screening for Major Depressive Disorder Compared With Structured Clinical Interview (KQ 2)

							Per 1,000 Screens Across a Prevalence From 3% to 11%	Per 1,000 Screens Across a Prevalence From 3% to 11%
Author, Year Quality	Age Range; Mean Age (SD), Years	Total N (% Female)	Index Test Cutoff	Prevalence (%)	Sensitivity	Specificity	No. False- Negatives	No. False- Positives
Beck Depression Inventor	y (BDI)							
Canals et al, 2001 ¹⁷⁰ Fair	17.5 to 18.5 18 (NR)	290 (50)	≥10 ≥11 ≥14 ≥16	Unclear	1.0 0.90 0.90 0.90	0.82 0.86 0.92 0.96	0 to 0 3 to 11 3 to 11 3 to 11	175 to 160 136 to 125 78 to 71 39 to 36
Roberts et al, 1991 ²³⁵ Fair	15 to 18* 16.6 (1.2)	1,704 (53)	≥11	3	0.84	0.81	5 to 18	184 to 169
Center for Epidemiologic S (CES-D)		sion						
Roberts et al, 1991 ²³⁵ Fair	15 to 18* 16.6 (1.2)	1,704 (53)	≥24		0.84	0.75	5 to 18	243 to 223
Garrison et al, 1991 ¹⁸⁹ Fair	12 to 15 NR	143 boys	≥12 ≥16 ≥20 ≥22	8.2	0.85 0.59 0.19 0.18	0.49 0.66 0.78 0.83	5 to 17 12 to 45 24 to 89 25 to 90	495 to 454 330 to 303 213 to 196 165 to 151
		189 girls	≥12 ≥16 ≥20 ≥22	8.7	0.84 0.83 0.84 0.83	0.38 0.53 0.70 0.77	5 to 18 5 to 19 5 to 18 5 to 19	601 to 552 456 to 418 291 to 267 223 to 205
Clinical Interview Schedul	e—Revised (CIS-	R)				-		
Patton et al, 1999 ²²³ Fair	NR [†] 15.7 (0.5)	158 (53 [‡])	NA§	6	0.18 (95% CI, 0.05 to 0.32)	0.97 (95% CI, 0.96 to 0.99) [¶]	25 to 90	29 to 27
Hopkins Symptom Checkl	ist (HSCL)							
Christensen et al, 2015 ¹⁷² Fair	14 to 16 NR	294 (NR)	≥9	11	0.85 (95% CI, 0.70 to 0.94)	0.78 (95% CI, 0.72 to 0.83)	5 to 17	213 to 196
Patient-Health Questionna								
Johnson et al, 2002 ¹⁹⁹ Fair	13 to 18 16 (1.2)	403 (63)	NA§	9	0.73 (calculated 95% CI, 0.58 to 0.85)	0.94 (calculated 95% CI, 0.91 to 0.96)	8 to 30	58 to 53

Table 3. Characteristics and Results of Test Accuracy Studies for Screening for Major Depressive Disorder Compared With Structured Clinical Interview (KQ 2)

							Per 1,000 Screens Across a Prevalence From 3% to 11%	Per 1,000 Screens Across a Prevalence From 3% to 11%			
Author, Year Quality	Age Range; Mean Age (SD), Years	Female)	Cutoff	Prevalence (%)	Sensitivity	Specificity	No. False- Negatives	No. False- Positives			
Pediatric Index of Emotional	Distress (PI-E	D) Depression	n Subscale								
O'Connor et al, 2016 ²¹⁹ Fair	8 to 17 12 (2.5)	135 (48)	≥8	11	0.94 (calculated 95% CI, 0.71 to 0.99)	0.81 (calculated 95% CI, 0.73 to 0.87)	2 to 7	184 to 169			
World Health Organization Fiv	World Health Organization Five Item Well-being Index (WHO-5)										
Christensen et al, 2015 ¹⁷² Fair	14 to 16 NR	294 (NR)	≥11	11	0.88 (95% CI, 0.74 to 0.96)	0.80 (95% CI, 0.74 to 0.84)	4 to 13	194 to 178			

^{*} This study enrolled persons in high school; 11% were younger than 15 and 13% were age 18 or older.

Abbreviations: BDI=Beck Depression Inventory; CES-D=Center for Epidemiological Studies-Depression; CI=confidence interval; CIS-R=Clinical Interview Schedule-Revised; KQ=key question; NA=not applicable; NR=not reported; PI-ED=Pediatric Index of Emotional Distress; SD=standard deviation; WHO-5=World Health Organization Five Item Well-being Index.

[†] The study targeted students in Year 9 of school.

[†] Proportion in the full study sample; not all were included in the diagnostic test accuracy analysis.

[§] Not applicable as test is scored according to an algorithm as either positive or negative.

Based on weighted adjustment; the unweighted sensitivity was 0.74.

[¶]Based on weighted adjustment; the unweighted specificity was 0.78.

Table 4. Key Characteristics of Included Suicide Risk Studies

Study Characteristics	Subcharacteristics	Number of Studies	Percent
Population characteristics:	Child (mean age <13, ages range from 5 to 12 years)	0	0
Child or adolescent	Adolescent (mean age ≥13, ages range from 11	16 ^{164, 179-182, 191-194,}	100
	to 19 years)	197, 200, 202, 212-215,	
	• ,	221, 222, 229, 236, 245, 265	
	Both (mean age varies, ages range from 5 to 19 years)	0	0
Population characteristics:	Mostly female	16 ^{164, 179-182, 191-194,}	100
•	•	197, 200, 202, 212-215,	
		221, 222, 229, 236, 245, 265	
Gender	Mostly male	0	0
Population characteristics:	Mostly White	11 ^{164, 191, 192, 194, 197,}	69
		200, 202, 212-215, 221,	
		222, 229, 236	
Race	Mostly non-White	1182	6
	Not reported	4 ¹⁷⁹⁻¹⁸¹ , 193, 245, 265	25
Population characteristics:	Suicide only	15 ^{164, 179-182, 191-194,}	94
		197, 200, 202, 212-215, 221, 222, 229, 236, 245, 265	
Diagnosis	Suicide and depression	1245	6
ntervention characteristics:	Nonpharmacological	16 ¹⁶⁴ , 179-182, 191-194, 197, 200, 202, 212-215,	100
		221, 222, 229, 236, 245, 265	
F f in f f in	Dhamaaalaniaal		
Types of interventions	Pharmacological Poth	0	0
Comparator	Both Treatment as usual	0 15 ^{164, 179-182, 191-193,}	0 94
Comparator	Treatment as usual	197, 200, 202, 212-215,	94
		221, 222, 229, 236, 245, 265	
	Attention control	1 ¹⁹⁴	6
Outcomes	Reporting benefits	16 ^{164, 179-182, 191-194,}	100
Jucomes	Reporting benefits	197, 200, 202, 212-215,	100
		221, 222, 229, 236, 245, 265	
	Reporting harms	2 ^{179-181, 192}	13
Geographic setting	United States of America	6164, 182, 194, 197, 200,	38
200grapino coming	ormod otatoo or runonod	202	00
	United Kingdom	6179-181, 191, 192, 221,	38
	5g	222, 236, 265	
	Australia	2 ^{193, 229}	13
	Norway	1 ²¹²⁻²¹⁵	6
	Taiwan	1 ²⁴⁵	6
Recruitment setting	Child and adolescent mental health services	5 ^{179-181, 191-193, 265}	31
<u> </u>	Emergency department	1,202	6
	Psychiatic outpatient	1 181, 212-215	6
	Schools	2 ^{197, 245}	13
	Combination	6 ^{164, 182, 194, 221, 222,}	38
		229, 236	
	Not specified	1 ²⁰⁰	6
Treatment setting	In person	11 164, 179-182, 191-193,	69
-		212-215, 221, 222, 229,	
		236, 265	
	Web/computer	1 ¹⁹⁴	6
	Combination (computer, in person, phone)	4 ^{197, 200, 202, 245}	25

Table 5. Suicide Attempts or Episode of Deliberate Self-Harm for Suicide or Self-Harm Interventions: Pooled Estimates

Intervention	Time of Outcome Measurement	Outcome Measure, Range, Threshold	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Family therapy, DBT, developmental	19 weeks to 18 months	Mean number of self-harm events	0.6 to 9.0	1.2 to 22.50	Mean difference: -0.76 (95% CI, -2.15 to 0.63); N=972; k=3; ^{179-181, 212-215, 265} \$\mu\$=68
group therapy					Appendix G Figure 2
Group psychotherapy, family therapy, mentalization- based treatment, developmental group therapy	6 to 18 months	Proportion with self-harm events	0.55 to 88	1.1 to 83	RR: 0.88 (95% CI, 0.63 to 1.24); N=1,040; k=5; ^{179-181, 191, 193, 236, 265} \$\ell^2=80\$ Appendix G Figure 3

Abbreviations: CI=confidence interval; DBT=dialectical behavior therapy; k=number of studies; $I^2=$ percentage of variation across studies that is due to heterogeneity rather than chance; N=number; OR=odds ratio.

Table 6. Suicidal Ideation for Suicide or Self-Harm Interventions: Pooled Estimates

Intervention	Time of Outcome Measurement	Outcome Measure, Range, Threshold	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Range at Followup	Comparator Range at Following	Pooled Results
Youth- nominated support team, motivational interviewing, DBT, IPT-A-IN	2 months to 19 weeks	BHS	0 to 20 ³⁰⁴	≥9 indicative of suicide intentions ³⁰⁴	5.66 to 7.74	7.80 to 12.42	Mean difference: -2.35 (95% CI, -4.06 to -0.65); N=644; k=4; ^{200, 202, 212-215,} ²⁴⁵ P=46% Appendix G Figure 4
Attachment- based family therapy, group psychotherapy, group therapy, youth- nominated support team, motivational interviewing, DBT, developmental group therapy	2 months to 71 weeks	SIQ or SIQ-Jr	SIQ: 0 to 180 SIQ-JR: 0 to 90 ³⁰⁵	SIQ ≥:41 ³⁰⁶ indicative of suicidal ideation SIQ-JR ³⁰⁷ ≥ 31 indicative of suicidal ideation	SIQ: 41.3 to 74.11 SIQ-JR: 5.2 to 25.55	SIQ: 39.7 to 76.40 SIQ-JR: 16.2 to 29.71	Standardized mean

^{*}Results standardized to pool across two different instruments.

Abbreviations: BHS=Beck Hopelessness Scale; CI=confidence interval; DBT=dialectical behavior therapy; IPT-A-IN=intensive interpersonal psychotherapy for depressed adolescents with suicidal risk; k=number of studies; l^2 =percentage of variation across studies that is due to heterogeneity rather than chance; N=number; SIQ=Suicidal Ideation Questionnaire; SIQ-Jr=Suicidal Ideation Questionnaire-Junior.

Table 7. Functioning for Suicide or Self-Harm Interventions: Pooled Estimates

Intervention	Time of Outcome Measurement	Outcome Measure, Range, Threshold	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Range at Followup	Pooled Results
Group psychotherapy; group therapy; developmental group therapy; psychoeducation for parents	8 weeks to 7 months	HoNOSCA	0 to 52 ³⁰⁸	Scores greater than 13 indicate impairment of clinical significance	8.4 to 16.8	6.9 to 17.6	Mean difference: -0.40 (95% CI, -2.55 to 1.78); N=509; k=4; ^{191,} 193, 229, 265 l^2 =56% Appendix G Figure 6
Therapeutic assessment; individual and family DBT; group therapy	8 to 71 weeks	CGAS	1 to 100 ³⁰⁹	>70: no clinically significant functional impairment <41: major impairment to functioning in several areas ³⁰⁹	58.5 to 65.7	60.1 to 64.22	Mean difference: 1.30 (95% CI, -2.52 to 5.12); N=195; k=3; ¹⁹³ , ²¹³ , ²²² P=30% Appendix G Figure 7

Abbreviations: CGAS=Children's Global Assessment Scale; CI=confidence interval; DBT=dialectical behavior therapy; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; N=number; RR=relative risk.

Table 8. Key Characteristics of Included Anxiety Studies for Benefits

Study Characteristics	Cub above staviation	Number of	Davaseri
Study Characteristics	Subcharacteristics	Studies	Percent
Population characteristics: Child or adolescent	Child (mean age <13)	24	82.7
	Adolescent (mean age ≥13)	5	17.39
Population characteristics: Gender	Mostly female	19	65.5
	Mostly male	9	31.0
	Equal distribution	1	3.4
Population characteristics: Race	Mostly White	17	58.6
	Mostly non-White	1	3.4
	Not reported	11	37.9
Population characteristics: Diagnosis	Any anxiety disorder	17	58.6
	GAD	5	17.2
	Social anxiety disorder	4	13.8
	Selective mutism	2	6.9
	GAD, social anxiety disorder, or separation anxiety	1	3.4
Intervention characteristics: Types of interventions	Nonpharmacological	22	75.9
	Pharmacological	6	20.7
	Multiple arms of CBT, pharmacotherapy, and combination	1	3.4
Comparator	Treatment as usual	2	6.9
•	Placebo comparator	7	24.1
	Wait-list comparator	20	69.0
Geographic setting	United States	10	34.5
	Australia	6	20.7
	United Kingdom	3	10.3
	Denmark	2	6.9
	Germany	2	6.9
	Norway	1	3.4
	Hong Kong	1	3.4
	Japan	1	3.4
	Spain	1	3.4
	Sweden	1	3.4
	Multiple countries	1	3.4
Recruitment setting*	Community recruitment	15	NA
	Referrals from mental health professionals	10	NA
	Schools	13	NA
	Not specified	2	NA

^{*} Studies may recruit from multiple settings.

Abbreviations: CBT=cognitive behavioral therapy; GAD=generalized anxiety disorder.

Table 9. Anxiety Interventions and Change in Anxiety Symptoms: Pooled Estimates of Effect

Intervention	Time of Outcome Measurement	Outcome Measure	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Psychotherapy	4	4 D 10 00D ()	2 / 2210	4.4			N
Individual or group Child-focused, child+parent focused, parent focused In person, email, telephone, or internet*	4 to 17 weeks from baseline	ADIS-CSR for the primary diagnosis or all diagnoses [†]	0 to 8 ³¹⁰	4 (moderate degree of impairment) or greater indicates a clinical diagnosis ³¹⁰	1.9 to 4.2	3.6 to 6.2	Mean difference: -2.01 (95% CI, -2.74 to -1.29); N=579; k=11; 163, 177, 178, 183, 196, 198, 224, 237, 242, 253, 275
Individual or group Child-focused, child+parent focused, parent focused In person, email, telephone, or internet§	6 to 17 weeks from baseline	SCAS-C	38 items rated on a 0 to 3 scale, maximum of 114	Cutoffs vary by age and gender from 33 to 50 ³¹¹ (higher scores represent worse outcomes)	21.6 to 34.9	29.4 to 42.1	Mean difference: -7.81 (95% CI, -10.99 to -4.63; N=668; k=9; 163, 177, 196, 198, 203, 206, 242, 246, 253 β=29% Appendix G Figure 13
Individual or group Child-focused, child+parent focused, parent focused In person, email, telephone, or internet§	6 to 17 weeks from baseline	SCAS-P	38 items rated on a 0 to 3 scale, maximum of 114	Cutoffs vary by age and gender from 33 to 50 ³¹¹ (higher scores represent worse outcomes)	18.8 to 33.1	24.2 to 41.3	Mean difference: -6.06 (95% CI, -9.58 to -2.56); N=652; k=9; 163, 177, 196, 198, 203, 206, 242, 246, 253 \$\rho = 58\%\$ Appendix G Figure 14
Individual or group Child-focused, child+parent focused In persont	6 to 17 weeks from baseline	SPAI-C	0 to 52 ³¹²	≥18 indicates social anxiety disorder ³¹²	12.5 to 15.5	22.8 to 30.8	Standardized mean difference¶: -1.17 (95% CI, -1.99 to -0.35); N=277; k=4; 165, 220, 239, 240, 275 \$\begin{align*} \ell^2 = 87\% \\ \text{Appendix G Figure 12} \end{align*}
Individual Child-focused or parent-led In person	5 to 12 weeks from baseline	CGI-S	1 to 7 ³¹³	2: borderline ill 3: mildly ill 4: moderate illness ³¹³	2.0 to 4.0	3.3 to 4.2	Mean difference: -0.60 (95% CI, -1.14 to -0.06); N=453; k=3; ^{190,} ^{237, 254-262} ρ =75% Appendix G Figure 9
Individual or group Child-focused, child+parent focused In person#	12 weeks from baseline	MASC	0 to 117	Unclear, ²⁷⁶ cutoff scores may not be possible to establish	40.9 to 48.8	42.9 to 54.7	Mean difference: -4.66 (95% CI, -9.66 to 0.34); N=435; k=3; ^{220, 251, 254-262, 275} β=66% Appendix G Figure 10
Individual or group Child-focused, child+parent focused In person, email, telephone, or internet**	10 to 12 weeks from baseline	RCMAS		≥19 ³¹⁴ indicates clinically significant levels of anxiety	6.6 to 10.9	9.8 to 15.7	Mean difference: -3.08 (95% CI, -5.91 to -0.24); N=241; k=3; 167, 206, 241 \$\mathcal{P}=71\%\$ Appendix G Figure 11

Table 9. Anxiety Interventions and Change in Anxiety Symptoms: Pooled Estimates of Effect

Intervention	Time of Outcome Measurement	Outcome Measure	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Pharmacotherapy	0.1.10		2 - 2215	=216		0.01.15.0	10 (050)
Fluoxetine, fluvoxamine, duloxetine, escitalopram, sertraline	8 to 12 weeks from baseline	PARS	0 to 25 ³¹⁵	>11.5 ³¹⁶ discriminates youth without	8.1 to 9.8	9.3 to 15.9	Mean difference: -4.0 (95% CI, -5.5 to -2.5); N=726; k=5; 168, 225-228, 243, 244, 254-262 \$\mathcal{P} = 81\%
				anxiety disorders from those with anxiety disorders			Appendix G Figure 16
Duloxetine, escitalopram, sertraline	8 to 12 weeks from baseline	CGI-S	1 to 7 ³¹³	2: borderline ill 3: mildly ill 4: moderate	2.4 to 3.0	3.1 to 3.9	Mean difference: -0.84 (95% CI, -1.13 to -0.55); N=550; k=4; ^{238, 243, 244, 254-262} P=75%
				illness ³¹³			Appendix G Figure 15

^{*} We averaged the results across arms for the two studies with multiple treatment arms (child directed or child and parent directed²²⁰ telephone vs. email vs. client initiated "on their own"²⁰⁶ compared with wait-list).

Abbreviations: ADIS-CSR=Anxiety Disorders Interview Schedule clinician severity ratings; CBT=cognitive behavioral therapy; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; I^2 =percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; MASC=Multidimensional Anxiety Scale for Children; N=number; PARS=Pediatric Anxiety Rating Scale; RCMAS=Revised Children's Manifest Anxiety Scale; SCAS-C=Spence Children's Anxiety Scale-Children's Scale-Children's Anxiety Scale-Parent-rated; SPAI-C=Social Phobia and Anxiety Inventory for Children.

[†] We selected or combined CSR ratings for primary diagnoses when available.

[‡] Pooled standardized mean differences that included all studies (including one reporting only Cohen's d estimates of effect²⁰⁶) also suggested a statistically significant difference (-1.17 [95% CI, -1.56 to -0.78]; N=676; k=12; *I*²=79%).

[§] We averaged the results across arms for the two studies with multiple treatment arms (brief vs. full CBT, 246 telephone vs. email vs. client initiated "on their own" compared with wait-list)

We averaged the results across arms for the two studies with multiple treatment arms (with or without cognitive restructuring, 240 child or child+parent 220, 275).

[¶]Reported as standardized mean difference because two of the did not present sufficient information to calculate mean differences.

[&]quot;We averaged the results across arms for the two studies with multiple treatment arms (child or child+parent, 220, 275 individual or group 251).

^{**} We averaged the results across arms for the two studies with multiple treatment arms (child directed or child and parent directed³¹⁷).

Table 10. Anxiety Interventions and Clinical Response, Remission From Anxiety, and Loss of Diagnosis: Pooled Estimates of Effect

	Time of	Outcome	0	Outcome Threshold	Treatment	Commenctor Donne	
Intervention	Outcome Measurement	Outcome Measure	Outcome Range	Indicating Clinically Meaningful Effect	Range at Followup	Comparator Range at Followup	Pooled Results
	Wicasurement	IVICa5u1C	Range	Wearingtui Enect	1 Ollowup	at i ollowup	Fooled Nesults
Psychotherapy Individual or group therapy	4 weeks to 6	Proportion with a	0 to 100	CGI-I scores of 1 or 2	40% to	0 to 37%	RR: 1.89 (95% CI, 1.17 to
Child-, parent-, or child+parent-	months from	clinical response	0 10 100	indicate moderate	83%	0 10 37 %	3.05); N=606; k=6; 178, 190, 195,
focused therapy	baseline	(CG1=1 or 2)		marked improvement,	0376		237, 253, 254 / 2=64%
In-person therapy	baseline	(001=1012)		proportion threshold			Appendix G Figure 17
in person incrapy				unclear			Appendix O Figure 17
Individual or group therapy	8 to 16 weeks	Remission from	0 to 100	Unclear "clinically	43% to	6% to 38%	RR: 2.68 (95% CI, 1.48 to
Child-, parent-, or child+parent-	from baseline	anxiety symptoms		significant change"	62%		4.88); N=321; k=4; ^{163, 198, 206,}
focused therapy		on child-rated					²⁴² / ² =48%*
In person, email, telephone,		SCAS					Appendix G Figure 18
internet therapy							
Individual, group, or	8 to 16 weeks	Loss of all anxiety	0 to 100	No diagnosis following	15% to	0 to 35%	RR: 3.09 (95% CI, 1.98 to
individual+group therapy	from baseline	diagnoses		a structured clinical	80%		4.80); N=1,414; k=15; 163, 167, 177, 183, 190, 195, 196, 198, 224, 241, 242,
Child-, parent-, or child+parent- focused therapy				interview			246, 251, 253 / ² =65% [†]
In person, telephone, internet							Appendix G Figure 19
therapy							Appelluix O ligure 19
Individual, group, or	6 weeks to 12	Loss of primary	0 to 100	No diagnosis following	7% to 80%	0 to 43%	RR: 3.02 (95% CI, 1.84 to
individual+group therapy	months from	anxiety diagnosis		a structured clinical			4.95); N=1,079; k=13; ^{163, 177} ,
Child-, parent-, or child+parent-	baseline	,,		interview			178, 183, 190, 196, 198, 220, 224, 242, 246,
focused therapy							^{251, 253, 275} / ² = 75% [‡]
In person, telephone, internet							Appendix G Figure 20
therapy							
Pharmacotherapy							
Escitalopram, fluoxetine,	8 to 12 weeks	Proportion with a	0 to 100 for	CGI-I scores of 1 or 2	50% to	9% to 44%	RR: 2.11 (95% CI, 1.58 to
sertraline	from baseline	clinical response	proportion	indicate moderate	91%		2.98); N=370; k=5; 168, 169, 238,
		(CGI=1 or 2)		marked improvement,			^{244, 254-262}
				proportion threshold			Appendix G Figure 21
				unclear			

^{*} We averaged the results across arms for one study with three intervention arms: telephone, email, and client-initiated CBT.²⁰⁶

Abbreviations: CBT=cognitive behavioral therapy; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; N=number; RR=relative risk; SCAS=Spence Children's Anxiety Scale.

[†] We averaged the results across arms for three studies with two intervention arms: individual and group CBT,²⁵¹ brief and full CBT,²⁴⁶ and child directed and child and family directed therapy.¹⁶⁷

^{*}We averaged the results across arms for three studies with two intervention arms: individual and group CBT, 251 brief and full CBT, 246 and child and child+parent CBT. 220, 275

Table 11. Anxiety Interventions and Functional Status: Pooled Estimates of Effect

Intervention	Time of Outcome Measurement	Outcome Measure	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Psychotherapy Individual or group therapy In person, internet or combined Child-, parent-, or child+parent- focused therapy	4 to 12 weeks from baseline	CGAS	1 to 100 ³⁰⁹	>70: no clinically significant functional impairment <41: major impairment to functioning in several areas ³⁰⁹	53.6 to 82.1	52.5 to 61.9	Mean difference: 7.54 (95% CI, 2.84 to 12.23); N=811; k=8; ^{178, 183, 190, 196, 224, 251, 253-262} β=90% Appendix G Figure 23
Individual or group therapy In person, telephone, internet or combined Child-, parent-, or child+parent- focused therapy	8 to 12 weeks from baseline	CAIS	0 to 81 ³¹⁸	<7: no anxiety diagnoses ³¹⁹	6.4 to 21.8	15.2 to 19.6	Mean difference: -2.23 (95% CI, -5.88 to 1.43); N=403; k=3; 246 . $^{253, 255}$ β =38% Appendix G Figure 22
Pharmacotherapy Duloxetine, fluoxetine, sertraline	10 to 12 weeks from baseline	CGAS	1 to 100 ³⁰⁹	>70: no clinically significant functional impairment <41: major impairment to functioning in several areas ³⁰⁹	62.1 to 68.5	59.3 to 64.6	Mean difference: 5.14 (95% CI, 3.21 to 7.08); N=551; k=3; 168, 243, 254-262 P=0% Appendix G Figure 24

Abbreviations: CAIS=Children's Anxiety Impact Scale; CGAS=Children's Global Assessment Scale; CI=confidence interval; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; N=number.

Table 12. Key Characteristics of Included Depression Studies for Benefits

Study Characteristics	Subcharacteristics	Number of Studies	Percent
Population characteristics: Child or adolescent	Child (mean age <13)	3	23.1
	Adolescent (mean age ≥13)	10	76.9
Population characteristics: Gender	Mostly female	11	84.6
·	Mostly male	2	15.4
Population characteristics: Race	Mostly White	7	53.8
	Mostly non-White	1	7.7
	Not reported	5	38.5
Population characteristics: Diagnosis*	MDD	13	100.0
	PDD/DD/DNOS	4	30.1
Intervention characteristics: Types of interventions	Nonpharmacological	8	61.5
	Pharmacological	2	15.4
	Multiple arms of CBT, pharmacotherapy, and combination	2	15.4
	Collaborative care	1	7.7
Comparator	Attention control	3	23.1
·	Placebo comparator	4	30.8
	Treatment as usual	4	30.8
	Wait-list comparator	2	15.4
Geographic setting	United States	10	76.9
	Sweden	3	23.1
Recruitment setting	Advertised widely	7	53.8
	Health systems and clinics	3	23.1
	Schools and mental health clinics	1	7.7
	Mental health clinics	1	7.7
	Not specified	1	7.7

^{*}Not mutually exclusive.

Abbreviations: CBT=cognitive behavior therapy; MDD=major depressive disorder; PDD/DD/DNOS=persistent depressive disorder/dysthymia disorder/depression not otherwise specified.

Table 13. Depression Interventions and Depression Symptoms: Pooled Estimates of Effect

	Time of			Outcome Threshold	Treatment	Comparator	
	Outcome	Outcome		Indicating Clinically	Range at	Range at	
Intervention	Measurement	Measure	Outcome Range	Meaningful Effect	Followup	Following	Pooled Results
Psychotherapy ³¹⁰							
Internet-based individual CBT group in-person CBT with and without parents, interpersonal psychotherapy*	8 to 12 weeks	BDI or BDI-II	BDI: 0 to 39 ²¹⁶ BDI-II: 0 to 63 ³²⁰	BDI: <10: minimal depression 10 to 18: mild to moderate depression 19 to 29: moderate to severe depression ≥30: severe depression ^{170, 235} BDI-II: 0–13: minimal depression 14–19: mild depression 20–28: moderate depression 29–63: severe depression ³²⁰	BDI: 8.4 to 13.3 BDI-II: 16 to 19.9	BDI: 12.3 to 16 BDI-II: 24.8 to 25.2	Standardized mean difference: -0.58 (95% CI,-0.83 to -0.34); N=471; k=4; \(^{174}, ^{216}, ^{248}, ^{249} \(^{\beta} = 0\)% Appendix G Figure 25
Individual in-person youth CBT, group in- person CBT with and without parents, interpersonal psychotherapy*	8 to 52 weeks from baseline	HAM-D	Unclear (2 studies ^{174, 175} used a 14-item version of HAM-D)	Unclear	4.9 to 8.7	6.5 to 12.8	Mean difference: -2.25 (95% CI,-4.09 to -0.41); N=262; k=3; ^{174,} ^{175, 216} \$\rho\$=0% Appendix G Figure 26
Individual in-person CBT, family CBT	12 to 52 weeks from baseline	CDRS-R	17 to 113 ³²¹	≥40 indicates depression ≤28 indicates remission (minimal or no symptoms ³²¹)	30.0 to 42.1	28.2 to 41.8	Mean difference: 0.77 (95% CI,-0.97 to 2.48); N=471; k=3; ^{176, 187, 207} \$\rho^2 = 0\%\$ Appendix G Figure 27
Pharmacotherapy							
Escitalopram, fluoxetine	8 to 12 weeks from baseline	CDRS-R	17 to 113 ³²¹	≥40 indicates depression ≤28 indicates remission (minimal or no symptoms ³²¹)	32.6 to 36.3	36.4 to 41.8	Mean difference: -3.76 (95% CI,-5.95 to -1.57); N=793; k=3; ^{185,} ^{207, 252} \$\mu\$=49% Appendix G Figure 28

^{*} We averaged the results across arms for the study with multiple treatment arms (group in-person CBT with or without parents¹⁷⁴) compared with wait-list.

Abbreviations: BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CI=confidence interval; CDRS-R=Children's Depression Rating Scale-Revised; CI=confidence interval; HAM-D=Hamilton Depression Rating Scale; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies: N=number.

[†] Mean differences standardized to pool BDI and BDI-II measures.

Table 14. Depression Interventions and Remission From Depression, and Loss of Diagnosis: Pooled Estimates of Effect

Intervention	Time of Outcome Measurement	Outcome Measure	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Psychotherapy							
CBT	8 to 12 weeks from baseline	Loss of diagnosis measured by clinical interviews	0 to 100 for proportion	NA	56% to 71%	16% to 60%	RR: 1.73 (95% CI, 1.00 to 3.00); N=395; k=4; ^{174, 207, 248, 249} / ² =81%* Appendix G Figure 29
Pharmacotherapy							
Escitalopram, fluoxetine	8 to 12 weeks from baseline	Remission from depression symptoms (CDRS- R≤28)	0 to 100 for proportion	CDRS-R≤28 indicates moderate marked improvement, proportion threshold unclear	23% to 46%	17% to 38%	RR: 1.20 (95% CI, 1.00 to 1.45), N=793; k=3; ^{185, 207, 210, 252} \$\mu\$=0% Appendix G Figure 30

^{*} We averaged the results across arms for one study with two intervention arms: with and without parent sessions. 174

Abbreviations: CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CI=confidence interval; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; NA=not applicable; RR=relative risk.

Table 15. Depression Interventions and Functional Status: Pooled Estimates of Effect

Intervention Psychotherapy	Time of Outcome Measurement	Outcome Measure	Outcome Range	Outcome Threshold Indicating Clinically Meaningful Effect	Treatment Range at Followup	Comparator Range at Following	Pooled Results
Individual in-person CBT, interpersonal psychotherapy	12 to 52 weeks from baseline	CGAS	1 to 100 ³⁰⁹	>70: no clinically significant functional impairment <41: major impairment to functioning in several areas ³⁰⁹	60.0 to 72.3	59.3 to 74.1	Mean difference: 1.52 (95% CI, -1.54 to 4.58); N=601; k=4;176,207,216 \$\mathcal{P}=66\%\$ Appendix G Figure 31
Pharmacotherapy Escitalopram, fluoxetine	8 to 12 weeks from baseline	CGAS	1 to 100 ³⁰⁹	>70: no clinically significant functional impairment <41: major impairment to functioning in several areas ³⁰⁹	62.1 to 68.5	59.3 to 64.6	Mean difference: 2.60 (95% CI, 0.78 to 4.42); N=793; k=3; ^{185, 207, 252} <i>P</i> =0% Appendix G Figure 32

Abbreviations: CBT=cognitive behavioral therapy; CGAS=Children's Global Assessment Scale; CI=confidence interval; *I*²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; N=number.

Table 16. Key Characteristics of Included Anxiety Studies for Harms

		Number of	_
Study Characteristics	Subcharacteristics	Studies	Percent
Population characteristics: Child or adolescent	Child (mean age <13)	6	54.5
	Adolescent (mean age ≥13)	5	45.5
Population characteristics: Gender	Mostly female	8	72.7
	Mostly male	2	18.2
	Equal distribution	1	9.1
Population characteristics: Race	Mostly White	8	72.7
	Not reported	3	27.3
Population characteristics: Diagnosis	Any anxiety disorder	3	27.3
	GAD	4	36.4
	Social anxiety disorder	1	9.1
	Selective mutism	1	9.1
	GAD, social anxiety disorder, or separation anxiety	2	18.2
Intervention characteristics: Types of interventions	Nonpharmacological	4	36.4
	Pharmacological	6	54.5
	Multiple arms of CBT, pharmacotherapy, and combination	1	9.1
Comparator	Placebo comparator	7	63.6
	Wait-list comparator	4	36.4
Geographic setting	United States	6	54.5
	United Kingdom	2	18.2
	Denmark	1	9.1
	Germany	1	9.1
	Multiple countries	1	9.1
Recruitment setting	Community recruitment	3	27.3
	Referrals from mental health professionals	5	45.5
	Schools	1	9.1
	Not specified	2	18.2

Abbreviations: CBT=cognitive behavioral therapy; GAD=generalized anxiety disorder.

Table 17. Key Characteristics of Included Depression Studies for Harms

Study Characteristics	Subcharacteristics	Number of Studies	Percent
Population characteristics: Child or adolescent	Child (mean age <13)	1	14.3
	Adolescent (mean age ≥13)	6	85.7
Population characteristics: Gender	Mostly female	7	100.0
	Mostly male	0	0.0
Population characteristics: Race	Mostly White	4	57.1
	Mostly non-White	0	0.0
	Not reported	3	42.9
Population characteristics: Diagnosis	MDD	7	100.0
	PDD/DD/DNOS	1	14.3
Intervention characteristics: Types of interventions	Nonpharmacological	2	28.6
	Pharmacological	3	42.9
	Multiple arms of CBT, pharmacotherapy, and combination	1	14.3
	Collaborative care	1	14.3
Comparator	Placebo comparator	3	42.9
•	Treatment as usual	2	28.6
	Placebo or another antidepressant	1	14.3
	Attention control	1	14.3
Geographic setting	United States	5	71.4
	Multiple countries	1	14.3
	Sweden	1	14.3
Recruitment setting	Advertised widely	3	42.9
	Health systems and clinics	2	28.6
	Not specified	2	28.6

Abbreviations: CBT=cognitive behavioral therapy; GAD=generalized anxiety disorder; MDD=major depressive disorder; PDD/DD/DNOS=persistent depressive disorder/dysthymia disorder/depression not otherwise specified.

Table 18. Summary of Outcomes

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 1 Benefits of screening	None	Not applicable	Not applicable	Not applicable	Insufficient	NA
KQ 2 Accuracy of screening	Suicide: 1 study (580)	Varies by reference standard Sensitivity range: 0.87 to 0.91 Specificity: 0.60	Consistency unknown, imprecise	Unclear whether thresholds were established a priori or whether interviewers were blinded; single study	Insufficient	Participants were potential high school dropouts; instrument was a 20-item screener embedded into a longer questionnaire so unclear whether feasible in primary care
	Anxiety: 10 studies 166, 171, 188, 199, 218, 219, 230-232, 250 (3,260)	Varies by screener, threshold, and condition Sensitivity range: 0.34 to 1.00 Specificity range: 0.47 to 0.99	Consistency unknown, imprecise	No replication of results for specific thresholds and screeners, unclear whether thresholds were established a priori or whether index and reference standard results were blinded	Low to moderate (varies by instrument)	Participants were primarily adolescents, but children were included in 4 studies. Applicable to both primary care and school-based settings. A variety of different screeners, only two are widely used in practice for detecting anxiety (i.e., SCARED and SPIN)
	Depression: 7 studies ^{170, 172, 189,} 199, 219, 223, 235 (3,316)	Varies by screener and threshold Sensitivity (excluding outliers) range: 0.59 to 0.94 Specificity range (excluding outliers): 0.38 to 0.96 PHQ-A: sensitivity, 0.73 (95% CI, 0.58 to 0.85); specificity, 0.94 (95% CI, 0.91 to 0.96)	Consistent when multiple studies are available, precise for specificity, precision varies for sensitivity	Unclear whether thresholds were established a priori or whether index and reference standard results were blinded; no replication of approaches for most screeners	Low to moderate for sensitivity (varies by instrument) Moderate for specificity	Primarily adolescents as only one study included children younger than age 12 years; seven different screeners evaluated but most not being used in practice; the most commonly cited instrument for use in current practice is PHQ-9

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 3 Harms of screening tests	Suicide: 2 RCTs ^{267, 268} (2,675)	No significant differences in measures of short-term distress/emotions for students exposed to suicide screening items compared with those not exposed (2	Consistent, precise	Fair-quality trials with some attrition; only evaluated	Low for no short- term harms from screening for suicide risk;	High school students; one study entirely comprised males
	Depression: 0 studies	RCTs)		measures of immediate and	insufficient for screening for	
	Anxiety: 0 studies	No significant differences in suicidal ideation between students exposed to screening items and those not exposed (1 RCT)		short-term emotions (over 1 to 2 days)	depression and anxiety	
KQ 4: Benefits of treatment	Suicide: 16 RCTs 164, 179-182, 191-194, 197, 200, 202, 212-215, 221, 222, 229, 236, 245, 265 (3,034)	Statistically significant difference favoring interventions on all deaths in the National Death Index (hazard ratio for treatment as usual: 6.62 [95% CI, 1.49 to 29.35]; N=448; k=1); Beck Hopelessness Scale (pooled mean difference: -2.35 (95% CI, -4.06 to -0.65); N=644; k=4; ℓ =46%); nonstatistically differences favoring suicide risk interventions on the SIQ and SIQ-Junior, mixed on other measures No statistically significant differences on suicide deaths, hospitalization or ED visits, number of self-harm events, proportion with self-harm events, or functioning	Consistent, imprecise	All interventions cannot mask treatment, leading to the potential for bias in outcome reporting; all comparison groups are TAU comparisons, which in many cases were quite active treatments and could bias results toward null effects	Psychotherapy Low for benefit for suicidal ideation and clinical response; insufficient for all other outcomes	Applicable to adolescents (predominantly females); no studies recruited children younger than age 11 years; most recruited from mental health or specialist settings

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 4: Benefits of treatment (continued)	Anxiety: 29 RCTs (22 on CBT, 6 on pharmaco- therapy, 1 on CBT, sertraline, and combination) ^{163,} 165, 167-169, 177, 178, 183, 190, 195, 196, 198, 203, 206, 220, 224-228, 237-244, 246, 251, 253- 262 (2,970)	CBT: Statistically significant differences favoring CBT on several pooled measures of symptom improvement, response (pooled RR: 1.89 [95% CI, 1.17 to 3.05]; N=606; k=5; \(\ell^2 = 64\% \)), remission (RR: 2.68 [95% CI, 1.48 to 4.88]; N=321; k=4; \(\ell^2 = 48\% \)), and loss of diagnosis (RRs range from 3.02 to 3.09) Statistically significant improvement on Children's Global Assessment Scale (pooled mean difference: 7.54 [95% CI, 2.84 to 12.23]; N=811; k=8; \(\ell^2 = 90\% \)) but not Children's Anxiety Impact Scale Pharmacotherapy: Statistically significant differences favoring pharmacotherapy on pooled measures of symptom improvement and response (RR: 2.11 [95% CI, 1.58 to 2.98]; N=370; k=5; \(\ell^2 = 18\% \)). Statistically significant differences favoring pharmacotherapy on pooled functional measure (Children's Global Assessment Scale): mean difference: 5.14 [95% CI, 3.21 to 7.08]; N=551; k=3; \(\ell^2 = 0\% \), but not other measures of functioning	CBT Mostly consistent, mostly precise Pharmaco- therapy Mostly consistent, mostly precise	Potential for bias from attrition, additionally CBT studies cannot mask treatments, leading to the potential for bias in outcome reporting	CBT: Moderate for anxiety symptoms, response, remission, and loss of diagnosis; low for functioning depending on the measure used Pharmacotherapy: Moderate for anxiety symptoms, response, remission, and loss of diagnosis; low for functioning depending on the measure used	15 CBT studies targeted any anxiety disorders; only 1 pharmacotherapy study targeted any anxiety disorders Studies addressed youth from ages 3 to 20 years, but 11 were conducted exclusively in adolescents Psychotherapy studies were limited to CBT; pharmacotherapy studies were limited to drugs with FDA approval for pediatric use

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 4: Benefits of treatment (continued)	Depression: 13 RCTs ^{174-176, 185,} 187, 204, 205, 207, 216, 233, 248, 249, 252, 266 (2 on pharmacotherapy; 9 on psychotherapy; 1 on CBT, fluoxetine, and combination; 1 on collaborative care) (2,156)	Psychotherapy: Varied by measure with some pooled estimates of effect favoring psychotherapy for symptoms (BDI or BDI-II standardized mean difference: -0.58 [95% CI,-0.83 to -0.34]; N=471; k=4; \(\tilde{P} = 0\)%; Hamilton Depression mean difference: -2.25 [95% CI,-4.09 to -0.41]; N=262; k=3; \(\tilde{P} = 0\)%), clinical response (3 studies with statistically significant results using varying thresholds), and loss of diagnosis (RR: 1.73 [95% CI, 1.00 to 3.00]; N=395; k=4; \(\tilde{P} = 81\)%), but other outcome measures do not consistently demonstrate a statistically significant difference Pharmacotherapy: Statistically significant differences favoring pharmacotherapy for one measure of symptoms (Children's Depression Rating Scale-Revised mean difference: -3.76 [95% CI, -5.95 to -1.57]; N=793; k=3; \(\tilde{P} = 49\)%) Pooled differences favor pharmacotherapy but are not statistically significant for remission Other outcome measures do not demonstrate a statistically significant difference Collaborative care: Statistically significant differences favoring collaborative care for symptoms at 6 months (CDRS-R change: 8.5 [95% CI, 13.4 to -3.6]; p=0.001), response by 12 months (OR for ≥50% reduction in CDRS-R score from baseline: 3.3 [95% CI, 1.4 to 8.2]); remission (OR for PHQ-9 <5 at 6 months: 5.2 [95% CI, 1.6 to 17.3]; no benefits for functioning)	Mostly consistent, Mostly imprecise	Psychotherapy cannot mask treatment, leading to the potential for bias in outcome reporting	Psychotherapy: Low for benefit for all outcomes other than remission Pharmaco- therapy: Low for benefit for all outcomes other than response Collaborative care: Low for benefit for symptoms, response, and remission Insufficient for functioning	Studies addressed youth from ages 3 to 19 years, but 9 were conducted exclusively in adolescents Pharmacotherapy studies were limited to drugs with FDA approval for pediatric use

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 5: Harms of treatment	Suicide: 2 RCTs ^{179, 192} (885)	No statistically significant differences on adverse events (such as attendance at minor injury units, walk-in centers, accident and emergency centers; re-referral to mental health service; and hospital attendance)	Consistent, imprecise	All interventions cannot mask treatment, leading to the potential for bias in outcome reporting; all comparison groups are TAU comparisons, which in many cases were quite active treatments and could lead to bias toward null effects	Insufficient	Applicable to adolescents, primarily females in these trials, both recruited from mental health or specialist settings
	Anxiety: 11 RCTs ^{168, 169, 224-} 228, 238, 239, 242-244, 253-262 (4 on CBT; 6 on pharmacotherapy; 1 on CBT, sertraline, and combination) (1,293)	Psychotherapy: Inconsistent results on suicide-related events; harms were events and not statistically significant Pharmacotherapy: More suicide-related events and withdrawals due to adverse events in the pharmacotherapy arm but harms were rare and not statistically significant	Consistent to mostly consistent, imprecise	All CBT interventions cannot mask treatment, leading to the potential for bias in outcome reporting	Psychotherapy: Insufficient evidence Pharmaco- therapy: Low for harms	2 of 4 CBT studies included any anxiety disorders; 1 of 7 pharmacotherapy studies included any anxiety disorders Studies addressed children from age 5 to 20 years, but 4 were conducted exclusively in adolescents Psychotherapy studies are limited to CBT, and pharmacotherapy studies are limited to drugs with FDA approval for pediatric use

Key Question	No. of Studies Study Designs (No. of Participants)	Summary of Findings	Consistency and Precision	Limitations	Strength of Evidence	Applicability
KQ 5: Harms of treatment (continued)	Depression: 6 RCTs ^{176, 185, 186,} 207-211, 233, 252, 266 and 1 meta- analysis ¹⁷³ (3 on pharmaco- therapy; 2 on psychotherapy; 1 on CBT, fluoxetine, and combination; 1 on collaborative care) (1,352 from trials)	Psychotherapy: Increased risk for suicide-related outcomes in one study, magnitude unclear due to inconsistent study reporting; no differences in negative effects in one trial Pharmacotherapy: Increased risk of suicide-related outcomes, withdrawal due to adverse events and serious adverse events, magnitude unclear due to inconsistent study reporting Collaborative care: Inconsistent results for psychiatric hospitalizations and emergency department visits	Consistent to inconsistent, imprecise	Psychotherapy trials cannot mask treatment, leading to the potential for bias in outcome reporting, inconsistent results across publications from one trial	Psychotherapy: Insufficient Pharmacotherapy: Low for harms Collaborative care: Insufficient	Studies addressed youth from ages 6 to 18 years, but 5 were conducted exclusively in adolescents Pharmacotherapy studies were limited to drugs with FDA approval for pediatric use.

Abbreviations: BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CI=confidence interval; ED=emergency department; FDA=Food and Drug Administration; I²=percentage of variation across studies that is due to heterogeneity rather than chance; k=number of studies; KQ=key question; MDD=major depressive disorder; N=number of participants; NA=not applicable; OR=odds ratio; PHQ-9=Patient Health Questionnaire-9; PHQ-A=Patient Health Questionnaire—Adolescent; RCT=randomized, controlled trial; RR=relative risk; SIQ=Suicidal Ideation Questionnaire; TAU=treatment as usual.

CQ 1: What is the diagnostic yield from screening for anxiety, depression, or increased suicide risk in typical primary care settings?

Given the seriousness of unmet mental health needs in youth, identification of depression, anxiety, and risk for suicide is critical. With nearly half of all youth birth to 17 years having access to healthcare in a medical home, ¹ primary care is a logical place for detecting these conditions in youth. Recent research has begun to examine the extent of screening for mental health disorders in pediatric primary care as well as the outcomes of screening, including diagnosis and referral. In addition to studies included for the key question on screening test accuracy (KQ 2), we examined recent literature on screening in primary care for depression (n=11),²⁻¹⁰ anxiety (n=1),¹¹ or suicide (n=2)^{4, 12} to describe the outcomes following a positive screening. Some of these studies reported on more than the focal mental health condition.

Screening for depression. The studies included for KQ 2 (screening test accuracy)¹³⁻¹⁹ each examined the prevalence of depression. However, only three of the seven studies recruited youth from primary care;¹³ in these three studies the prevalence of depression across varied populations ranged from 8.2 percent to 11 percent. We included seven additional studies that did not meet criteria for KQ 2 studies of accuracy but that had relevant information for examining the outcome of depression screening in primary care settings.^{2-4, 6, 9, 10, 20} Only one of these studies¹⁰ provided data that permitted us to calculate the prevalence of depression. Thus, we report the positive predictive value (PPV) to describe the yield of diagnosing depression following a positive screen.

Appendix A Table 1 details the outcome of a positive screen reported in these studies, all of which included one of the PHQ versions (i.e., PHQ-A, PHQ-9, PHQ-9M). Three studies^{6, 10, 20} reported the diagnosis of depression following a positive screen, and two of these studies^{6, 10} found that depression diagnoses increased after implementing an intervention designed to improve the rate of depression screening. The Bose study¹⁰ found that the rate of depression diagnoses went from 1 percent before their intervention to 13 percent afterward and to 39 percent of those with a positive screen. 10 Although the rate of diagnosed depression did not increase in the Lewandowski study, the number of adolescents (134) diagnosed with depression tripled over the three waves of the study; in the last year of their study, the rate of depression diagnosis following a positive screen was 36 percent. Importantly, neither the Bose nor Lewandowski studies had control groups. The Stafford study reported that of the adolescents who had a positive screen, 71 percent received a diagnosis of depression. ²⁰ One additional study, ² reported that 20% of the youth who screened positive on the PHQ-9 were not depressed as indicated on medical chart abstraction, but it is not clear whether they or the remaining 80% underwent a formal depression diagnosis. Although the remainder of the studies ^{2-4, 9, 10, 20} did not diagnose depression directly, they made referrals to mental health providers, which may have included diagnosis along with service provision. However, this is unknown.

Screening for anxiety. Among the 10 studies included for KQ 2 (screening test accuracy), only four recruited youth in primary care settings. 13, 21-23 The prevalence of anxiety disorders across varied populations in these four studies ranged from 2.5 percent to 13 percent. Only one additional study reported on implementation of a screening program in primary care that was designed to detect anxiety disorders and mental health utilization. 11 Although the study administered the SCARED and SAS screeners as well as clinical interviews via telephone, the

investigators did not report any data that examined the rate of anxiety disorders in relation to screening data. Prevalence rates determined from the interviews with 190 parents using the ADIS were 3.2 percent for GAD, 6.8 percent for a social anxiety disorder, and 16.8 percent for any anxiety disorder. The detection rates from screening and rates of anxiety disorder from a clinical interview were similar, but the positive predictive value of the two screening measures is unknow, because, as noted above, the investigators did not report any data that examined the rate of anxiety disorders in relation to screening.

Screening for suicide. In the single study included for KQ 2 (screening test accuracy), the prevalence of high suicide risk among a population of potential high school dropouts recruited from seven high schools in the Pacific Northwest region of the United States was between 19 and 22 percent depending on the reference standard used.²⁴ Two studies that were not eligible for inclusion in KO 2, because they did not have an eligible comparator, provided additional information about detection of persons at high risk for suicide in primary care^{4, 12} The Etter study screened for suicidality with a single question as well as for depression using the PHQ-9.¹² In the sample of over 2.134 youth, 131 (6%) endorsed suicidality. Providers documented followup actions for all but 20 of the youth. Of the remaining 109 youth, providers indicated that 93 were not suicidal after provider assessment, suggesting that of those who endorsed the suicidality question, 15 percent were at high risk for suicide. The Farley study, 4 which was primarily a study to assess identification and management of adolescent depression in a large pediatric care network, administered the PHO-9 along with two optional suicide risk questions. They found that 597 (8.6%) of the 6,923 adolescents completing the screener were flagged for suicide risk, but they did not examine followup for this group, other than to report that all but 230 (17%) had elevated depression scores on the PHQ. They did report that 15 of the 1,797 youth with elevated PHO depression scores were deemed to be at high risk of suicide, and they followed emergency procedures for these youth. If these youth were part of the 498 with elevated scores who were also flagged for suicide risk, then the rate of high suicide risk in those who endorsed suicide questions is 3 percent; however, there is no information about the 99 adolescents flagged for suicide risk who had PHQ scores in the normal range.

The takeaway from this group of studies is that few studies conducted in primary care address the prevalence of anxiety, depression, or elevated risk of suicide or the rates of diagnosing these disorders after a positive screen.

CQ 2: What are the minimal clinically important differences (the smallest value of benefit to patients) for symptoms and functioning on the most common instruments used to measure response to treatment of depression, anxiety, or suicide risk?

Recent systematic reviews on anxiety²⁵ and depression²⁶ have noted the lack of research in minimal clinically important differences. A supplemental search of PubMed for this systematic review yielded no relevant citations for children with depression, anxiety, or suicide risk; systematic reviews on the topic also confirmed the lack of evidence.²⁷ The depression review relied on distribution-based methods (that is, methods based on statistical properties of the distribution of outcome measures²⁸) for judging minimal clinically important differences, due to the lack of anchor-based methods (that is, methods based on direct questioning of patients,

providers, or caregivers). Distribution-based methods do not account for patient preferences²⁸ or identify any particular values for minimal clinically important differences (MCID); rather, they indicate that values above and below prespecified units of standard deviations are likely not important or not minimal.²⁹ In the absence of these MCID values, information about the established thresholds for the outcome measures offers some basis for judging whether the results are clinically meaningful. Tables 5, 6, 7, 9, 11, 13, and 15 in the main report lists these thresholds for pooled analyses along with a range of values for the treatment and comparison arms.

CQ 3: What are the U.S. Food and Drug Administration boxed warnings for pharmacotherapy for the treatment of depression, anxiety, or suicide risk in children and adolescents?

The current Food and Drug Administration (FDA) boxed warning, contraindications, pediatric warnings, and pediatric use statements for all drugs included in this review are shown below in Appendix A Table 2. The FDA issued a boxed warning for children and adolescents for all antidepressants in 2004 based on an FDA-conducted pooled analysis that found increased risk of suicidality when pooling across all antidepressants and all indications. All drugs used in studies included in this review were selective serotonin reuptake inhibitors (SSRIs) and carry a boxed warning stating that there is "[i]ncreased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders." Some warnings contain extra guidance stating that prescribers should "monitor for worsening and emergence of suicidal thoughts and behaviors."

SSRIs as a class may be associated with a higher risk of serious adverse events among adolescents and children with MDD and with a higher risk of withdrawal due to adverse events among adolescents with MDD. A 2020 comparative effectiveness review found paroxetine, which was excluded from this current USPSTF review update because it is not FDA approved for children or adolescents, may be associated with a higher risk of suicidal ideation or behaviors in adolescents with MDD. The evidence from the comparative effectiveness review was insufficient for other SSRIs as a drug class across populations and depressive disorders for outcomes related to suicide. ²⁶

The FDA has approved two SSRIs to treat MDD in children or adolescents (fluoxetine for children age 8 years or older and escitalopram for adolescents ages 12 to 17 years).

CQ 4: What psychotherapies other than cognitive behavioral therapy are used to treat anxiety in children?

CBT has the largest evidence base for treatment of anxiety disorders in children. Several other less well-studied interventions have been evaluated for treating anxiety in children and adolescents.

Nine RCTs reported on attention bias modification treatment (ABMT) as a psychotherapy to treat anxiety disorders in children and adolescents. 31-39 ABMT is based on the theory that attention training toward positive stimuli can reduce anxiety. The protocol uses a computerized dot-probe task to assess the individual's threat bias and then to treat the bias by systematically

redirecting attention away from the threat stimuli.⁴⁰ Across this body of evidence, two RCTs^{32, 39} found some benefit for treatment of anxiety disorders with ABMT,^{32, 39} while six RCTs^{31, 33-38} found no significant benefit of the intervention in decreasing anxiety.

Other interventions to treat anxiety in children have a smaller evidence base. One RCT⁴¹ compared 10 weeks of acceptance and commitment therapy (ACT) to CBT to wait-list control in 193 children with anxiety disorder diagnoses and found that ACT and CBT were both superior to wait-list control and gains were maintained at 3 months post treatment. ACT and CBT produced similar outcomes. Psychodynamic psychotherapy is another intervention that has been less well studied, but one RCT⁴² was found comparing psychodynamic psychotherapy treatment (PDT) to CBT and wait-list control in 107 adolescents with social anxiety disorder ages 14 through 20 years. Both PDT and CBT were superior to wait-list control.

CQ 5: What is the effectiveness of evidence-based treatment in children and adolescents with persistent depressive disorder and depressive disorders not otherwise specified?

The recent AHRQ Effective Health Care systematic review on the effectiveness of treatment for depression in children and adolescents noted that the evidence base is sparse for persons with persistent depressive disorder (PDD) and depressive disorders not otherwise specified (DDNOS) and varies by age and disorder. This review found insufficient evidence to evaluate the effectiveness of pharmacological treatments for PDD or DDNOS among children and adolescents. Regarding nonpharmacological approaches, family therapy and CBT compared with wait-list or active control may improve symptoms, response, and functional status among children or adolescents with PDD or DDNOS. The strength of evidence for all outcomes is low. The rest of this section describes studies that were included for this evidence based on the AHRQ EHC review. EHC review.

One RCT⁴³ with medium risk of bias compared family-based interpersonal therapy (IPT) with active control in children (ages 7 to 12 years) with a range of depressive disorders including PDD and DDNOS in a 14-week intervention. Family-based IPT improved clinician-, self-, and parent-reported depressive symptoms. The mean difference on the clinician-reported scale (CDRS-R) was -0.50 (95% CI, -2.48 to 0.10). The mean difference on the self-reported Mood and Feelings Questionnaire for Children (MFQ-C) was -6.50 (95% CI, -7.85 to 5.15). The mean difference on the parent-reported Mood and Feelings Questionnaire (MFQ-P) was -5.60 (95% CI, -6.49 to 4.71). The authors of the AHRQ EHC review concluded that the evidence was insufficient to judge the effectiveness of family-based IPT when compared with active control for remission.²⁶

Two RCTs, one with high risk of bias⁴⁴ and one with some⁴⁵ risk-of-bias concerns, compared CBT with wait-list control among adolescents with a range of depressive disorders including PDD. The duration of the intervention spanned 8⁴⁵ to 12⁴⁴ weeks. Compared with wait-list control, CBT improved self-reported depressive symptoms (mean difference [Beck Depression Inventory (BDI)], -5.90 [95% CI, -10.89 to -0.92]) and improved clinician-reported functional impairment (mean difference [Global Assessment of Functioning (GAF)], 6.5 [95% CI, 0.68 to 12.32]). The authors of the AHRQ EHC review concluded that the evidence was insufficient to

judge whether there were improvements noted in clinician- or parent-reported depressive symptoms, recovery, or response.²⁶

Three RCTs, two with some risk-of-bias concerns⁴⁶⁻⁴⁸ and a third with high risk of bias,⁴⁹ that included children and adolescents (ages 7 to 18 years) compared family therapy with active control in studies that were 8 to 16 weeks long. Compared with active control, one study⁴⁶ found that family therapy showed higher rates of adequate clinical depression response with a 50 percent reduction in CDRS-R scores from baseline to posttreatment (risk difference, 179/1,000 [95% CI, 25 more cases to 333 more cases]). The authors of the AHRQ EHC review concluded that the evidence was insufficient to evaluate the effectiveness of family therapy and active control for clinician- or self-reported depressive symptoms, depression response, remission, recurrence, and clinician- or self-reported functional impairment.²⁶

The existing evidence base offers limited indication of benefit for children and adolescents with PDD or DDNOS. The lack of evidence on pharmacological treatments and on the effects of interventions in children stand out as gaps and may serve as areas for future research. In addition, new research should establish minimally important differences to help understand the trade-offs between benefits and harms. Well-designed trials will contribute to a stronger body of evidence and greater certainty in the estimate of effectiveness.

Our update search for the USPSTF review update yielded no additional relevant citations to this contextual question.

CQ 6: What proportion of children and adolescents who screen positive for depression, anxiety, or increased suicide risk engage with care (i.e., return for clinical evaluation and treatment)?

We identified five studies that addressed followup for those screening positive for depression.^{4,} ⁵⁰⁻⁵² One retrospective chart review of three large healthcare systems (two health maintenance organization and one network of community health centers) found that of 4,612 adolescents newly screened positive for depression in primary care, 854 (19%) received no followup visit of any type within the following 3 months. Of those who did have at least one visit, 824 (22%) did not have depression symptoms addressed. The remaining 2,934 (78%) were started on therapy (n=1,315), antidepressant medication (n=891), or combined therapy (n=728). Of those started on antidepressants, 356 (40%) did not have a followup within 3 months.⁵⁰

Another study of 16-year-old patients screened for depression with the PHQ-9M at one of 31 sites of a large pediatric primary care practice found an association between more severe depression and increased likelihood to followup.⁴ Of 466 patients with a PHQ-9M score of 11 to 27, 349 (75.4%) had followup of some type (depression diagnosis, behavioral health referral, medication, or repeated PHQ-9) within the following year.⁴ Of the 1,331 patients screening positive for more mild depression (PHQ-9M score of 5 to 10), only 530 (39.9%) had followup of some sort.⁴

One study of 10 primary care clinics screening for depression using PHQ-2/PHQ-9 found that of the 796 patients with a PHQ-9 score of 10 or more, 638 were referred to behavioral health treatment and only 370 (58%) engaged in such treatment.⁵¹

One study of adolescents screening for psychiatric illness (oppositional defiant disorder, attention deficit hyperactivity disorder, depression, suicide, anxiety, separation, and others) using the Mini International Neuropsychiatric Interview (MINI) screener in an emergency room found that 200 screened positive.⁵³ All who screened positive were given a referral to a mental health provider, and less than 2 percent of those patients had followed up with a mental health provider when asked during telephone followup after 6 weeks.⁵³

Only one identified study looked at followup rates of those screening positive for suicide, in this case from an urgent care clinic setting. Patients 12 years or older were routinely screened by nursing using a two-question screener. If positive, a social worker administered the Columbia Suicide Severity Rating Scale (C-SSRS). Of 75 adolescents screening positive on the C-SSRS, 10 were admitted into psychiatric inpatient care, four were admitted to medical inpatient units, one left against medical advice, one was transferred to the emergency department, and 59 were referred to mental health professionals. Of those 59 referred to mental health professionals, it is not documented how many actually accessed care.⁵⁴

No identified studies examined followup after screening positive for anxiety.

Taken together, these studies suggest that many adolescents who screen positive for depression in primary care will engage in treatment of some type and will be more likely to followup if screening positive for more severe depression. While not definitive, these studies suggest that likelihood of following up may be higher if screened in primary care rather than emergency department settings. This may be a factor of continuity, of primary care or mental health access and availability, or of other unseen factors.

Appendix A Table 1. Outcomes of Depression Screening

			Positive	Depression	
Study	N	Screener	Screen	Diagnoses	Referral
Aalsma et al, 2018 ²	2,038	PHQ-2 then PHQ-9	303 (15%)	NA	128 (42%)
Bose et al, 2021 ¹⁰	73	PHQ-A (cutoff ≥5)	29 (40%)	12 (45%)*	9.2% [†]
Chowdhury et al, 2020 ³	1,213	PHQ-9 (cutoff ≥5)	96 (8%)	NA	42 (44%)
Farley et al, 20204	10,713	PHQ-9M (cutoff ≥5)	1,797 (17%)	NA	449 (25%)
Lewandowski et al, 2016 ⁶	2,283	PHQ-9	435 (19%)	134 (36%)‡	NA
Stafford et al, 2020 ²⁰	80§	PHQ-2 then PHQ-9	80§	57 (74%)	10 (12%)
		(cutoff ≥9)			
Sudhanthar et al, 20159	NA	PHQ-2 then PHQ-9	NA	NA	38% increase¶

^{*}No information provided regarding diagnostic procedure for depression.

Abbreviations: NA=not available; PHQ=Patient Health Questionnaire.

[†]The number of individuals who were referred and what the 9.2% represents were unclear.

[†]Of those with incident-positive PHQ-9.

[§]Study only included adolescents who screened positive for depression.

Of those who were managed in primary care.

No n's were reported.

Appendix A Table 2. FDA Boxed Warnings for Medication Included in Updated Review of Screening for Anxiety, Depression, and Suicide Risk in Children and Adolescents

Name of Drug	Date Searched	Date on FDA Label	Boxed Warning	Contraindications	Pediatric Warnings	Pediatric Use Statements
Clomipramine ⁵⁵		March 2019	Yes	History of hypersensitivity to clomipramine or other tricyclic antidepressants, use of MAOIs, use of linezolid or intravenous methylene blue, and those in acute recovery period from myocardial infarction.	None	Clomipramine hydrochloride is not approved for use in pediatric patients except for patients with obsessive compulsive disorder (OCD).
	February 9, 2021	December 2008	Yes	It should not be used concomitantly or in close temporal proximity with a MAOI or in patients with uncontrolled narrow-angle glaucoma.	Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for MDD and other psychiatric disorders.	Not approved for use in pediatric patients.
Escitalopram ⁵⁷	February 11, 2021	January 2017	Yes	It should not be used concomitantly or within 14 days of an MAOI. It should not be used concomitantly with linezolid, intravenous methylene blue, or pimozide, or in patients with known hypersensitivity to escitalopram or citalopram or any of the inactive ingredients.	Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for MDD and other psychiatric disorders.	Approved for acute and maintenance treatment of MDD in adolescents ages 12 to 17 years Not approved for use in patients younger than 12 years. Safety and effectiveness have not been established in pediatric patients younger than 18 years with generalized anxiety disorder.
	February 11, 2021	January 2017	Yes	It should not be used concomitantly or within 5 weeks of an MAOI or thioridazine. It should not be used concomitantly with linezolid, intravenous methylene blue, or pimozide. If used in combination with olanzapine, the contraindications for Symbyax should also be observed.	Increased risk of suicidal thinking and behavior in children, adolescents, and young adults taking antidepressants for MDD and other psychiatric disorders. Monitor for worsening and emergence of suicidal thoughts and behaviors.	Approved for use in pediatric patients with MDD and OCD. Safety and effectiveness in patients younger than 8 years with MDD and younger than 7 years with OCD have not been established. Safety and effectiveness in combination with olanzapine in patients younger than 10 years for depressive episodes associated with bipolar I disorder have not been established.

Appendix A Table 2. FDA Boxed Warnings for Medication Included in Updated Review of Screening for Anxiety, Depression, and Suicide Risk in Children and Adolescents

		Date on FDA				
Name of Drug	Searched	Label	Warning	Contraindications	Pediatric Warnings	Pediatric Use Statements
Fluvoxamine ⁵⁹	February 11,	April	Yes	It should not be used concomitantly	Increased risk of suicidal thinking and	Not approved for use in
	2021	2008		or within 14 days of an MAOI. It	behavior in children, adolescents, and	pediatric patients except
				should not be used concomitantly	young adults taking antidepressants	those with OCD.
				with tizanidine, thioridazine,	for MDD and other psychiatric	
				alosetron, or pimozide.	disorders.	
Sertraline ⁶⁰	February 11,	December	Yes	It should not be used concomitantly	Increased risk of suicidal thoughts and	Safety and effectiveness in
	2021	2016		or within 14 days of an MAOI. It	behaviors in pediatric and young adult	pediatric patients other than
				should not be used concomitantly	patients. Closely monitor for clinical	those with OCD have not
				with pimozide or disulfiram (oral	worsening and emergence of suicidal	been established.
				solution only) or in patients with	thoughts and behaviors.	
				known hypersensitivity to sertraline or		
				excipients.		

Abbreviations: FDA=Food and Drug Administration; MAOI=monoamine oxidase inhibitor; MDD=major depressive disorder; OCD=obsessive compulsive disorder.

Appendix A Table 3. Screening and Engagement With Care

Study #	Screening Tool	Setting	Diagnosis(es) Addressed in Followup Statistics	Followup Rates
O'Connor et al, 2016 ⁵⁰	PHQ-9	3 healthcare centers	Depression	Of 4,612 screened positive or newly diagnosed with depression, 854 (19%) did not engage in followup of any kind. Of the 891 started on antidepressants at followup, 356 (40%) had no subsequent followup within 3 months.
Farley et al, 2020 ⁴	PHQ-9M	31 sites of pediatric primary care practice in U.S. mid-Atlantic region		466 had PHQ-9M score 11–27 349 (75.4%) had followup of some type in the following year 1,331 had score of 5–10 530 (39.9%) had mental health followup of some type
Thompson et al, 2018 ⁵¹	PHQ-2/PHQ-9	10 primary care clinics	Depression	Of 796 that had a PHQ-9 of 10 or above, 638 were referred to additional services, of which 370 (58%) were engaged in treatment
Downey et al, 2018 ⁵³	MINI	Emergency department	Suicide, depression, ODD, ADHD, anxiety, separation	41% of 200 children screened positive for some sort of psychiatric illness. All were referred to mental health provider and <2% of patients had followed up when asked via telephone followup in 6 weeks
Patel et al, 2018 ⁵⁴	2-question screener, followed by C-SSRS by social worker	Urgent care	Suicide	Of 75 positive C-SSRS screens, 10 psychiatric admissions, 4 medical admissions, 1 left against medical advice, 1 transfer to emergency department, and 59 were referred to mental health (with no indication from this study of followup from there)

Abbreviations: ADHD=attention-deficit/hyperactivity disorder; C-SSRS=Columbia Suicide Severity Rating Scale; MINI= Mini International Neuropsychiatric Interview; ODD=oppositional defiant disorder; PHQ=Patient Health Questionnaire; PHQ-2=Patient Health Questionnaire-2 questions; PHQ-9=Patient Health Questionnaire-9 questions; PHQ-9M= Patient Health Questionnaire-9 questions Modified; U.S.=United States.

MEDLINE® via PubMed

Suicide Risk: January 1, 2012, through April 28, 2020

Anxiety: January 1, 2017 to April 28, 2020 Depression: June 1, 2012 to April 28, 2020

Search	Query	Results
1	"Depressive Disorder" [MeSH] OR "Depressive Disorder, Major" [MeSH] OR Depression [MeSH] OR depress* [Title/Abstract] OR depression [Title/Abstract] OR depressive [Title/Abstract] OR depressed [Title/Abstract] OR "Dysthymic Disorder" [Mesh] OR dysthymia OR dysthymic OR "Persistent Depressive Disorder" [ALL FIELDS]	496,379
2	Mass Screening[MeSH] OR screen[tiab] OR screening[tiab] OR screened[tiab] OR screens[tiab] OR "case finding"[tiab] OR casefinding[tiab] OR "beck depression inventory" OR "beck depression inventories" OR "Center for Epidemiologic Studies Depression Scale"[All Fields] OR "Center for Epidemiologic Studies Depression Scales"[All Fields] OR "depression inventory"[tiab] OR "depression inventories"[tiab] OR "depression scales"[tiab] OR "depression rating scales"[tiab] OR "depression rating scales"[tiab] OR "depression rating scales"[tiab] OR "mood and feelings questionnaire"[All Fields] OR "mood and feelings questionnaires"[All Fields] OR "Patient Health Questionnaire-Adolescent Version"[All Fields] OR Reynold*[tiab] OR "self report rating scales"[All Fields] OR BDI[tiab] OR CES-D[tiab] OR ChilD-S[tiab] OR DesTeen[tiab] OR MFQ-SF[tiab] OR PHQ-2[tiab] OR PHQ-A[tiab] OR RCDS[tiab]	862,015
3	#1 AND #2	69,492
4	#1 AND #2 Filter: from 2015 - 2020	26,844
5	#1 AND #2 Filter: English, from 2015 - 2020	26,092
6	#1 AND #2 Filter: English, Child: birth-18 years, from 2015 - 2020	4,688
7	adolescen*[tiab] OR boys[tiab] OR child*[tiab] OR children[tiab] OR girls[tiab] OR pediatric[tiab] OR paediatric*[tiab] OR teen[tiab] OR teens[tiab] OR teenage[tiab] OR teenaged[tiab] OR teenager*[tiab] OR toddler*[tiab]	1,737,521
8	#5 AND #7	4,576
9	#6 OR #8	6,839
10	address[pt] OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR "case reports"[pt] OR "case reports"[tw] OR "case reports"[tw] OR "case series"[tw] OR "case series"[tw] OR "comment"[pt] OR congress[pt] OR "dictionary"[pt] OR "directory"[pt] OR "editorial"[pt] OR "festschrift"[pt] OR "historical article"[pt] OR "interview"[pt] OR lecture[pt] OR "legal case"[pt] OR "legislation"[pt] OR letter[pt] OR "newspaper article"[pt] OR "patient education handout"[pt] OR "periodical index"[pt] OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] OR cow[tw] OR cows[tw] OR chicken[tw] OR chickens[tw] OR horse[tw] or horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep OR ovine OR murine OR murinae	10,206,468
11	#9 NOT #10	6,741

Appendix B. Search Strategies

Search	Query	Results
12	"Anti-Anxiety Agents" [Mesh] OR "Antidepressive Agents" [Mesh] OR "Serotonin Uptake Inhibitors" [Mesh] OR "Tranquilizing Agents" [Mesh] OR antidepressant* [tiab] OR "antidepressives" [tiab] OR "antidepressive agents" [tiab] OR "antidepressive drug" [tiab] OR "antidepressive drugs" [tiab] OR "norepinephrine reuptake inhibitor" [all fields] OR "norepinephrine reuptake inhibitors" [all fields] OR "selective serotonin reuptake inhibitor" [tiab] OR "selective serotonin reuptake inhibitors" [tiab] OR ssriftiab] OR ssris [tiab] OR "serotonin norepinephrine reuptake inhibitors" [All Fields] OR "serotonin norepinephrine reuptake inhibitors" [All Fields] OR "TCA antidepressants" [All Fields] OR "tricyclic antidepressants" [All Fields] OR anafranil [All Fields] OR cleas [tiab] OR Citalopram [Mesh] OR citalopram [tiab] OR clomipramine [Mesh] OR clomipramine [Mesh] OR clomipramine [Mesh] OR secitalopram [tiab] OR Fluoxetine [Mesh] OR fluoxetine [Mesh] OR ketamine [Mesh] OR luvox [tiab] OR "Lithium Compounds/therapeutic use" [Mesh] OR lithium [tiab] OR luvox [tiab] OR Sertraline [Mesh] OR sertraline [Mesh] OR Zoloft [tiab]	246,639
13	#1 AND #12	68,565
16	"Behavior Therapy"[MeSH] OR "Cognitive Behavioral Therapy"[Mesh] OR "Combined Modality Therapy"[Mesh] OR Counseling[MeSH] OR "Delivery of Health Care, Integrated"[Mesh] OR "Directive Counseling"[MeSH] OR "Family Therapy"[MeSH] OR "Parents/education"[MeSH] OR "Patient Care Management"[Mesh] OR "Problem Solving"[MeSH] OR Psychotherapy[MeSH] OR "Psychotherapy, Group"[MeSH] OR "Risk Reduction Behavior"[Mesh] OR "Self-Help Groups"[MeSH] OR (behavior*[tiab] AND (therap*[tiab] or treatment*[tiab] OR intervention*[tiab])) OR CBT[tiab] OR (cognitive[tiab] AND (therap*[tiab] OR treatment*[tiab] OR intervention*[tiab])) OR "care delivery"[tiab] OR "care management"[tiab] OR "collaborative care"[tiab] OR "combination therapy"[tiab] OR "combined modality"[tiab] OR counsel*[tiab] OR "delivery of care"[tiab] OR "dialectical behavior therapy"[All fields] OR "family therapy"[tiab] OR "family support"[tiab] OR interpersonal therap*[tiab] OR interpersonal intervention*[tiab] OR "means restriction"[tiab] OR "means restrictions"[All Fields] OR "problem solving"[tiab] OR "psychoeducation"[tiab] OR psychotherap*[tiab] OR (risk*[tiab] AND reduc*[tiab]) OR "self help"[tiab]	2,120,901
17	#1 AND #16	99,177
18	#13 OR #17	148,472
19	#13 OR #17 Filter: from 2015 - 2020	44,779
20	#13 OR #17 Filter: English, from 2015 - 2020	43,229
21	#13 OR #17 Filter: English, Child: birth-18 years, from 2015 - 2020	6,611
22	#20 AND #7	6,389
23	#21 OR #22	9,511
24	#23 NOT #10	8,910
25	"cochrane database syst rev"[ta] OR "systematic review"[ti] OR "meta-analysis"[pt] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab] OR "meta-synthesis"[tiab] OR "meta-syntheses"[tiab] OR "systematic literature review"[ti] OR ("systematic review"[tiab] AND review[pt]) OR "this systematic review"[tw] OR "umbrella review"[tiab]	270,232
26	#24 AND #25	543
27	#24 NOT #26	8,367
29	"Anxiety Disorders"[Mesh] OR "Anxiety"[Mesh] OR agoraphobia OR anxiety[ti] OR "generalized anxiety disorder" OR mutism OR "panic disorder" OR phobia* OR "separation anxiety disorder" OR "social anxiety disorder"	169,198

Search	Query	Results
30	"Mass Screening" [MeSH] OR screen[tiab] OR screening[tiab] OR screened[tiab] OR screens[tiab] OR "case finding" [tiab] OR casefinding[tiab] OR "Children's Manifest Anxiety Scale" [All Fields] OR "Multidimensional Anxiety Scale for Children" [All Fields] OR "Pediatric Anxiety Rating Scale" [All Fields] OR "Revised Children's Manifest Anxiety Scale" [All Fields] OR "Screen for Child Anxiety Related Disorders" [All Fields] OR "Spence's Children's Anxiety Scale" [All Fields] OR "State-Trait Anxiety Inventory for Children" [All Fields] OR "Youth Anxiety Measure for DSM-5" [All Fields] OR MASC[tiab] OR "MASC-2 SR" [All Fields] OR MASC-10[tiab] OR PARS[tiab] OR RCMAS[tiab] OR SCARED[tiab] OR SCAS-8[tiab] OR STAIC[tiab] OR STAIC[tiab] OR STAIC-S[tiab]	802,488
31	#29 AND #30	8,121
32	#29 AND #30 Filter: English	7,694
33	#29 AND #30 Filter: English, Child: birth-18 years	2,684
34	#32 AND #7	1,992
35	#33 OR #34	3,092
36	#35 NOT #10	3,010
37	#29 AND #12	16,939
39	#29 AND #16	45,405
40	#37 OR #39	56,846
41	#37 OR #39 Filter: English	50,283
42	#37 OR #39 Filter: English, from 2017 - 2020	8,320
43	#37 OR #39 Filter: English, Child: birth-18 years, from 2017 - 2020	1,986
44	#42 AND #7	1,818
45	#43 OR #44	2,619
46	#45 NOT #10	2,389
47	#46 AND #25	147
48	#46 NOT #47	2,242
49	"Suicide"[Mesh] OR "Suicide, Attempted"[Mesh] OR "Suicide, Completed"[Mesh] OR "Suicidal Ideation"[Mesh] OR parasuicid*[ti] OR "self harm"[ti] OR "Self-Injurious Behavior"[Mesh] OR suicid*[ti]	77,404
50	"Mass Screening" [MeSH] OR screen[tiab] OR screening[tiab] OR screened[tiab] OR screens[tiab] OR "case finding" [tiab] OR casefinding[tiab] OR "Adapted-SAD PERSONS" [All Fields] OR "Beck Hopelessness Scale" [All Fields] OR "Beck Scale for Suicide Ideation" [All Fields] OR "Center for Epidemiologic Studies-Depression Scale" [All Fields] OR "Child Suicide Assessment" [All Fields] OR "Columbia Suicide Severity Rating Scale" [All Fields] OR "Columbia Teen Screen" [All Fields] OR "Firestone Assessment of Self-Destructive Thoughts" [All Fields] OR "Harkavy Asnis Suicide Survey" [All Fields] OR "Inventory for Suicidal Ideation" [All Fields] OR "Multiattitude Suicide Tendency Scale for Adolescents" [All Fields] OR "Paykel Suicide Items" [All Fields] OR "Positive and Negative Suicide Ideation Inventory" [All Fields] OR "Scale for Suicide Ideation" [All Fields] OR "Self-harm behavior questionnaire" [All Fields] OR "Suicide Behaviors Questionnaire" [All Fields] OR "Suicidal Ideation Questionnaire" [All Fields] OR "Suicidality Occurring in Paediatrics-Suicidality Assessment Scale" [All Fields] OR "Suicide Assessment Five-Step Evaluation and Triage" [All Fields] OR "Suicide Probability Scale" [All Fields] OR BSI[tiab] OR CESD [tiab] OR CSA[tiab] OR C-SSSR[tiab] OR CTS[tiab] OR SBQ-14[tiab] OR SBQ-C[tiab] OR SIQ[tiab] OR SIQ-Junior[tiab] OR STOP-SAS[tiab] OR SAFE-T[tiab] OR SPS[tiab] OR SRS[tiab]	837,759
51	#49 AND #50	3,485

Search	Query	Results
52	#49 AND #50 Filter: English	3,320
53	("2012/06/01"[Date - Publication] : "2020/12/31"[Date - Publication]) Filter: English	8,460,381
54	#52 AND #53	1,951
55	#52 AND #53 Filter: Child: birth-18 years	681
56	#54 AND#7	235
57	#55 OR #56	810
58	#57 NOT #10	786
59	#49 AND #12	4,971
60	#49 AND #16	15,458
61	#59 OR #60	18,818
62	#59 OR #60 Filter: English	16,713
63	#62 AND #53 Filter: English	6,314
64	#62 AND #53 Filter: English, Child: birth-18 years	2,143
65	#63 AND #7	1,511
66	#64 OR #65	2,569
67	#66 NOT #10	2,403
68	#67 AND #25	102
69	#67 NOT #68	2,301
70	"Pediatric Symptom Checklist-17" OR PSC[tiab] OR "Revised Children's Anxiety and Depression Scale"[All Fields] OR RCADS[tiab] OR RCADS-25[tiab] OR "Strength and Difficulties Questionnaires"[All Fields] OR SDQ[tiab]	8,116
71	(#1 OR #29 OR #49) AND #70	432
72	(#1 OR #29 OR #49) AND #70 Filter: English	421
73	(#1 OR #29 OR #49) AND #70 Filter: English, Child: birth-18 years	231
74	#72 AND #7	284
75	#73 OR #74	306
76	#75 NOT #10	300

Cochrane Library

Suicide Risk: January 1, 2012, through April 28, 2020

Anxiety: January 1, 2017 to April 28, 2020 Depression: June 1, 2012 to April 28, 2020

Search	Query	Results
1	[mh "Depressive Disorder"] or [mh "Depressive Disorder, Major"] or [mh Depression] or depress*:ti,ab or depression:ti,ab or depressive:ti,ab or depressed:ti,ab or [mh "Dysthymic Disorder"] or dysthymia:ti,ab,kw or dysthymic:ti,ab,kw or "Persistent Depressive Disorder":ti,ab,kw	75575
2	[mh "Mass Screening"] OR screen:ti,ab OR screening:ti,ab OR screened:ti,ab OR screens:ti,ab OR "case finding":ti,ab OR casefinding:ti,ab OR "beck depression inventory" OR "beck depression inventories" OR "Center for Epidemiologic Studies Depression Scale":ti,ab,kw OR "Center for Epidemiologic Studies Depression Scales":ti,ab,kw OR "depression inventory":ti,ab OR "depression inventories":ti,ab OR "depression scale":ti,ab OR "depression scales":ti,ab OR "depression rating scales":ti,ab OR "depression rating scales":ti,ab OR "mood and feelings questionnaires":ti,ab,kw OR "mood and feelings questionnaires":ti,ab,kw OR "Patient Health Questionnaire-Adolescent Version":ti,ab,kw OR Reynold*:ti,ab OR "self report rating scales":ti,ab,kw OR BDI:ti,ab OR CES-D:ti,ab OR ChilD-S:ti,ab OR DesTeen:ti,ab OR MFQ-SF:ti,ab OR PHQ-2:ti,ab OR PHQ-A:ti,ab OR RCDS:ti,ab	82010
3	#1 AND #2	20931
4	Address:pt OR "autobiography":pt OR "bibliography":pt OR "biography":pt OR "case control" OR "case report" OR "case reports" OR "case series" OR "comment":pt OR "comment on" OR congress:pt OR "cross-sectional" OR "dictionary":pt OR "directory":pt OR "editorial":pt OR "festschrift":pt OR "historical article":pt OR "interview":pt OR lecture:pt OR "legal case":pt OR "legislation":pt OR letter:pt OR "news":pt OR "newspaper article":pt OR "patient education handout":pt OR "periodical index":pt OR "retrospective cohort" OR ([mh "Animals"] NOT [mh "Humans"]) OR rats OR cow OR cows OR chicken OR chickens OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murine	64667
5	#3 NOT #4	20194
6	MeSH descriptor: [Child] explode all trees	2623
7	MeSH descriptor: [Infant] explode all trees	16136
8	MeSH descriptor: [Adolescent] explode all trees	101062
9	adolescen*:ti,ab OR boys:ti,ab OR child*:ti,ab OR children:ti,ab OR girls:ti,ab OR pediatric:ti,ab OR paediatric*:ti,ab OR teen:ti,ab OR teens:ti,ab OR teenage:ti,ab OR teenage:ti,ab OR teenaged:ti,ab OR teenager*:ti,ab OR toddler*:ti,ab	146691
10	#6 OR #7 OR #8 OR #9	235130
11	#5 AND #10	3330

Search	Query	Results
12	[mh "Anti-Anxiety Agents"] OR [mh "Antidepressive Agents"] OR [mh "Serotonin Uptake Inhibitors"] OR [mh "Tranquilizing Agents"] OR antidepressant*:ti,ab OR "antidepressive agents":ti,ab OR "antidepressive drug":ti,ab OR "antidepressive drugs":ti,ab OR "norepinephrine reuptake inhibitor":ti,ab,kw OR "norepinephrine reuptake inhibitors":ti,ab,kw OR "selective serotonin reuptake inhibitor":ti,ab OR "selective serotonin reuptake inhibitors":ti,ab OR ssri:ti,ab OR ssri:ti,ab OR ssri:ti,ab OR ssri:ti,ab OR "serotonin norepinephrine reuptake inhibitors":ti,ab,kw OR "TCA antidepressants":ti,ab,kw OR "tricyclic antidepressants":ti,ab,kw OR anafranil:ti,ab,kw OR celexa:ti,ab OR [mh Citalopram] OR citalopram:ti,ab OR [mh clomipramine] OR clomipramine:ti,ab OR [mh duloxetine] OR duloxetine:ti,ab OR [mh Fluoxetine] OR fluoxetine:ti,ab OR [mh Fluoxetine] OR ketamine:ti,ab OR [mh Sertraline] OR sertraline:ti,ab OR Zoloft:ti,ab OR [mh Sertraline] OR sertraline:ti,ab OR Zoloft:ti,ab	35486
13	#1 AND #12	16373
14	[mh "Behavior Therapy"] OR [mh "Cognitive Behavioral Therapy"] OR [mh "Combined Modality Therapy"] OR [mh Counseling] OR [mh "Delivery of Health Care, Integrated"] OR [mh "Directive Counseling"] OR [mh "Family Therapy"] OR [mh "Parents"/ED] OR [mh "Patient Care Management"] OR [mh "Problem Solving"] OR [mh Psychotherapy] OR [mh "Psychotherapy, Group"] OR [mh "Risk Reduction Behavior"] OR [mh "Self-Help Groups"] OR (behavior*:ti,ab AND (therap*:ti,ab or treatment*:ti,ab OR intervention*:ti,ab)) OR CBT:ti,ab OR (cognitive:ti,ab AND (therap*:ti,ab OR treatment*:ti,ab OR intervention*:ti,ab)) OR "care delivery":ti,ab OR "care management":ti,ab OR "collaborative care":ti,ab OR "combination therapy":ti,ab OR "combined modality":ti,ab OR counsel*:ti,ab OR "delivery of care":ti,ab OR "dialectical behavior therapy":ti,ab,kw OR "family therapy":ti,ab OR "family support":ti,ab OR interpersonal therap*:ti,ab OR interpersonal intervention*:ti,ab OR "means restriction":ti,ab OR "means restrictions":ti,ab,kw OR "mentalization therapy":ti,ab,kw OR (parent*:ti,ab AND education:ti,ab) OR "problem solving":ti,ab OR "psychoeducation":ti,ab OR psychotherap*:ti,ab OR (risk*:ti,ab AND reduc*:ti,ab) OR "self help":ti,ab	242343
15	#1 AND #14	29310
16	#13 OR #15	4188
17	#16 AND #10	7668
18	#17 NOT (clinicaltrials or trialsearch):so	5975
19	#11 NOT (clinicaltrials or trialsearch):so	2345
20	[mh "Anxiety Disorders"] OR [mh "Anxiety"] OR agoraphobia OR anxiety:ti OR "generalized anxiety disorder" OR mutism OR "panic disorder" OR phobia* OR "separation anxiety disorder" OR "social anxiety disorder"	23453
21	[mh "Mass Screening"] OR screen:ti,ab OR screening:ti,ab OR screened:ti,ab OR screens:ti,ab OR "case finding":ti,ab OR casefinding:ti,ab OR "Children's Manifest Anxiety Scale":ti,ab,kw OR "Multidimensional Anxiety Scale for Children":ti,ab,kw OR "Pediatric Anxiety Rating Scale":ti,ab,kw OR "Revised Children's Manifest Anxiety Scale":ti,ab,kw OR "Screen for Child Anxiety Related Disorders":ti,ab,kw OR "Spence's Children's Anxiety Scale":ti,ab,kw OR "State-Trait Anxiety Inventory for Children":ti,ab,kw OR "Youth Anxiety Measure for DSM-5":ti,ab,kw OR MASC:ti,ab OR "MASC-2 SR":ti,ab,kw OR MASC-10:ti,ab OR PARS:ti,ab OR RCMAS:ti,ab OR SCARED:ti,ab OR SCAS:ti,ab OR SCAS:ti,ab OR STAIC-S:ti,ab OR YAM-5:ti,ab	66544
22	#20 AND #21	1372
23	#22 AND #10	503
24	#23 NOT (clinicaltrials or trialsearch):so	345
	<u>I</u>	I

Search	Query	Results
25	#20 AND (#12 OR #14)	12437
26	#25 AND #10	3535
27	#26 NOT (clinicaltrials or trialsearch):so	3022
28	[mh "Suicide"] OR [mh "Suicide, Attempted"] OR [mh "Suicide, Completed"] OR [mh "Suicidal Ideation"] OR parasuicid*:ti OR "self harm":ti OR [mh "Self-Injurious Behavior"] OR suicid*:ti	2323
29	[mh "Mass Screening"] OR screen:ti,ab OR screening:ti,ab OR screened:ti,ab OR screens:ti,ab OR "case finding":ti,ab OR casefinding:ti,ab OR "Adapted-SAD PERSONS":ti,ab,kw OR "Beck Hopelessness Scale":ti,ab,kw OR "Beck Scale for Suicide Ideation":ti,ab,kw OR "Center for Epidemiologic Studies-Depression Scale":ti,ab,kw OR "Child Suicide Assessment":ti,ab,kw OR "Columbia Suicide Severity Rating Scale":ti,ab,kw OR "Columbia Teen Screen":ti,ab,kw OR "Firestone Assessment of Self-Destructive Thoughts":ti,ab,kw OR "Harkavy Asnis Suicide Survey":ti,ab,kw OR "Inventory for Suicidal Ideation":ti,ab,kw OR "Multi-attitude Suicide Tendency Scale for Adolescents":ti,ab,kw OR "Paykel Suicide Items":ti,ab,kw OR "Positive and Negative Suicide Ideation Inventory":ti,ab,kw OR "Scale for Suicide Ideation":ti,ab,kw OR "Self-harm behavior questionnaire":ti,ab,kw OR "Suicide Behaviors Questionnaire":ti,ab,kw OR "Suicidal Ideation Questionnaire":ti,ab,kw OR "Suicide Behaviors Questionnaire":ti,ab,kw OR "Suicidality Occurring in Paediatrics-Suicidality Assessment Scale":ti,ab,kw OR "Suicide Probability Scale":ti,ab,kw OR BSI:ti,ab OR CES-D:ti,ab OR CSA:ti,ab OR C-SSSR:ti,ab OR CTS:ti,ab OR HASS-II:ti,ab OR ISO-30:ti,ab OR PANSI:ti,ab OR SSI:ti,ab OR SHBQ:ti,ab OR SBQ-14:ti,ab OR SBQ-C:ti,ab OR SIQ:ti,ab OR SRS:ti,ab OR	72731
30	#28 AND #29	336
31	#30 AND #10	118
32	#31 NOT (clinicaltrials or trialsearch):so	85
33	#28 AND (#12 OR #14)	1577
34	#33 AND #10	527
35	#34 NOT (clinicaltrials or trialsearch):so	427

Psychinfo

Suicide Risk: January 1, 2012, through April 30, 2020

Anxiety: January 1, 2017 to April 30, 2020 Depression: June 1, 2012 to April 30, 2020

#	Query	Limiters/Expanders	Results
S1	DE "Depression (Emotion)" OR DE "Major Depression" OR DE "Anaclitic Depression" OR DE "Dysthymic Disorder" OR DE "Reactive Depression" OR DE "Recurrent Depression" OR DE "Treatment Resistant Depression" OR depressive OR depression OR depressed OR dysthymic OR dysthymia	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	360,288
S2	DE "Health Screening" OR DE "Screening Tests" OR screen OR screening OR screened OR screens OR "case finding" OR casefinding OR "beck depression inventory" OR "beck depression inventories" OR "Center for Epidemiologic Studies Depression Scale" OR "Center for Epidemiologic Studies Depression Scales" OR "depression inventory" OR "depression inventories" OR "depression scale" OR "depression scales" OR "depression rating scales" OR "Kutcher* OR "mood and feelings questionnaire" OR "mood and feelings questionnaires" OR "Patient Health Questionnaire-Adolescent Version" OR Reynold* OR "self report rating scales" OR BDI OR CES-D OR ChilD-S OR DesTeen OR MFQ-SF OR PHQ-2 OR PHQ-A OR RCDS	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	230,416
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	128,078
S4	S3	Limiters - Publication Year: 2015-2020; English; Language: English; Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	38,863
S5	S4	Limiters - Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs) Search modes - Boolean/Phrase	7,802
S6	PZ Abstract Collection OR PZ Bibliography OR PZ Clarification OR PZ Column/Opinion OR BK Conference Proceedings OR PZ Comment/Reply OR PZ Dissertation OR PT Dissertation Abstract OR PZ Editorial OR PT Enclyclopedia OR PZ Encyclopedia Entry OR PZ Interview OR PZ Letter OR PZ Obituary OR PZ Poetry OR "case control" OR "case report" OR "case reports" OR "case series" OR "comment on" OR "cross-sectional" OR "retrospective cohort" OR rats OR cow OR cows OR chicken OR chickens OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murine OR murinae	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	1,120,371
S7	S5 NOT S6	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	6,788

#	Query	Limiters/Expanders	Results
	DE "Tranquilizing Drugs" OR DE "Antidepressant Drugs" OR DE "Serotonin Norepinephrine Reuptake Inhibitors" OR DE "Serotonin Reuptake Inhibitors" OR antidepressant* OR "antidepressives" OR "antidepressive agents" OR "antidepressive drug" OR "antidepressive drugs" OR "norepinephrine reuptake inhibitor" OR "norepinephrine reuptake inhibitors" OR "selective serotonin reuptake inhibitor" OR "selective serotonin reuptake inhibitor" OR "serotonin norepinephrine reuptake inhibitor" OR "serotonin norepinephrine reuptake inhibitors" OR "serotonin norepinephrine reuptake inhibitors" OR "TCA antidepressants" OR "tricyclic antidepressants" OR "tricyclic antidepressants" OR "tricyclic antidepressants" OR anafranil OR celexa OR DE "Citalopram" OR citalopram OR DE "Chlorimipramine" OR clomipramine OR duloxetine OR escitalopram OR DE "Fluoxetine" OR fluoxetine OR DE "Fluoxeamine" OR fluoxetine OR DE "Ketamine" OR ketamine OR Lexapro OR lithium OR luvox OR DE "Sertraline" OR sertraline OR Zoloft	Search modes - Boolean/Phrase	71,843
S9	S1 AND S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	42,787
S10	DE "Behavior Therapy" OR DE "Cognitive Behavior Therapy" OR DE "Counseling" OR DE "Community Counseling" OR DE "Cross Cultural Counseling" OR DE "Educational Counseling" OR DE "Group Counseling" OR DE "Microcounseling" OR DE "Psychotherapeutic Counseling" OR (TX integrated AND DE "Health Care Delivery") OR DE "Family Therapy" OR DE "Strategic Family Therapy" OR DE "Interpersonal Psychotherapy" OR DE "Mentalization" OR DE "Psychoeducation" OR DE "Structural Family Therapy" OR (DE "Parents" AND TX education) OR DE "Treatment Planning" OR DE "Caring Behaviors" OR DE "Problem Solving" OR DE "Psychotherapy" OR DE "Group Psychotherapy" OR DE "Self-Help Techniques" OR (behavior* AND (therap* or treatment* OR intervention*)) OR CBT OR (cognitive AND (therap* OR treatment* OR intervention*)) OR "care delivery" OR "care management" OR "collaborative care" OR "combination therapy" OR "combined modality" OR counsel* OR "delivery of care" OR "dialectical behavior therapy" OR "family therapy" OR "family support" OR interpersonal therap* OR interpersonal intervention* OR "means restrictions" OR "mentalization therapy" OR (parent* AND education) OR "problem solving" OR "psychoeducation" OR psychotherap* OR (risk* AND reduc*) OR "self help"	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	1,084,659
S11	S1 AND S10	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	131,338
S12	S9 OR S11	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	157,878
S13	S12	Limiters - Publication Year: 2015-2020; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase	6,570

#	Query	Limiters/Expanders	Results
S14	S13 NOT S6	Search modes -	5,405
045		Boolean/Phrase	40.000
S15		Limiters - Methodology: -	43,300
		Systematic Review,	
		META ANALYSIS,	
		METASYNTHESIS	
		Search modes -	
S16	S14 AND S15	Boolean/Phrase Expanders - Apply	165
010	OTT AND OTO	equivalent subjects	103
		Search modes -	
		Boolean/Phrase	
S17	S14 NOT S16	Expanders - Apply	5,240
		equivalent subjects Search modes -	
		Boolean/Phrase	
S18	DE "Agoraphobia" OR DE "Anxiety" OR DE "Anxiety Disorders" OR DE	Expanders - Apply	147,222
	"Generalized Anxiety Disorder" OR DE "Mutism" OR DE "Elective	equivalent subjects	
	Mutism" OR DE "Obsessive Compulsive Disorder" OR DE "Panic	Search modes -	
	Attack" OR DE "Panic Disorder" OR DE "Phobias" OR DE "Separation Anxiety" OR DE "Separation Anxiety Disorder" OR DE "Social Anxiety"	Boolean/Phrase	
	OR DE "Social Phobia" OR DE "Trichotillomania" OR agoraphobia OR		
	TI anxiety OR "generalized anxiety disorder" OR mutism OR "panic		
	disorder" OR phobia* OR "separation anxiety disorder" OR "social		
0.10	anxiety disorder"		405.040
S19	DE "Health Screening" OR DE "Screening Tests" OR screen OR screening OR screened OR screens OR "case finding" OR casefinding	Expanders - Apply equivalent subjects	135,018
	OR "Children's Manifest Anxiety Scale" OR "Multidimensional Anxiety	Search modes -	
	Scale for Children" OR "Pediatric Anxiety Rating Scale" OR "Revised	Boolean/Phrase	
	Children's Manifest Anxiety Scale" OR "Screen for Child Anxiety		
	Related Disorders" OR "Spence's Children's Anxiety Scale" OR "State- Trait Anxiety Inventory for Children" OR "Youth Anxiety Measure for		
	DSM-5" OR MASC OR "MASC-2 SR" OR MASC-10 OR PARS OR		
	RCMAS OR SCARED OR SCAS OR SCAS-8 OR STAIC OR STAIC-S		
	OR YAM-5		
S20	S18 AND S19	Expanders - Apply	9,564
		equivalent subjects Search modes -	
		Boolean/Phrase	
S21	S20	Limiters - English;	3,977
		Language: English;	
		Age Groups:	
		Childhood (birth-12 yrs), Adolescence	
		(13-17 yrs);	
		Population Group:	
		Human	
		Search modes - Boolean/Phrase	
S22	S21 NOT S6	Limiters - English;	3,377
		Language: English;	-,
		Age Groups:	
		Childhood (birth-12	
		yrs), Adolescence (13-17 yrs);	
		Population Group:	
		Human	
		Search modes -	
		Boolean/Phrase	

#	Query	Limiters/Expanders	Results
S23	S18 AND (S8 OR S10)	Search modes -	62,758
		Boolean/Phrase	
S24	S23	Limiters - Publication Year: 2017-2020; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17	1,687
		yrs); Population Group: Human Search modes - Boolean/Phrase	
S25	S24 NOT S6	Search modes - Boolean/Phrase	1,434
S26	S25	Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase	55
S27	S25 NOT S26	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	1,379
S28	DE "Attempted Suicide" OR DE "Head Banging" OR DE "Self-Inflicted Wounds" OR DE "Self-Injurious Behavior" OR DE "Self-Mutilation" OR DE "Self-Poisoning" OR DE "Suicidal Ideation" OR DE "Suicidality" OR DE "Suicide" OR parasuicid*:ti OR "self harm":ti OR suicid*:ti	Search modes - Boolean/Phrase	47,432
S29	DE "Health Screening" OR DE "Screening Tests" OR screen OR screening OR screened OR screens OR "case finding" OR casefinding OR "Adapted-SAD PERSONS" OR "Beck Hopelessness Scale" OR "Beck Scale for Suicide Ideation" OR "Center for Epidemiologic Studies-Depression Scale" OR "Child Suicide Assessment" OR "Columbia Suicide Severity Rating Scale" OR "Columbia Teen Screen" OR "Firestone Assessment of Self-Destructive Thoughts" OR "Harkavy Asnis Suicide Survey" OR "Inventory for Suicidal Ideation" OR "Multiattitude Suicide Tendency Scale for Adolescents" OR "Paykel Suicide Items" OR "Positive and Negative Suicide Ideation Inventory" OR "Scale for Suicide Ideation" OR "Self-harm behavior questionnaire" OR "Suicide Behaviors Questionnaire" OR "Suicidal Ideation Questionnaire" OR "Suicidality Occurring in Paediatrics-Suicidality Assessment Scale" OR "Suicide Assessment Five-Step Evaluation and Triage" OR "Suicide Probability Scale" OR BSI OR CES-D OR CSA OR C-SSSR OR CTS OR HASS-II OR ISO-30 OR PANSI OR SSI OR SHBQ OR SBQ-14 OR SBQ-C OR SIQ OR SIQ-Junior OR STOP-SAS OR SAFE-T OR SPS OR SRS	Search modes - Boolean/Phrase	145,902
S30	S28 AND S29	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	5,110

S31 S30 Limiters - Published Date: 20120601 20201231 : English Language English Age Groups Childhood (birth-12 yrs), Adolescence (13-17 yrs) Population Group Human Expanders - Apply equivalent subjects Saarch modes - Boolean/Phrase Saarch modes - Saarch modes - Boolean/Phrase Saarch modes - Saarch m	#	Query	Limiters/Expanders	Results
Date: 20120601 20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolbescence (13-17 yrs); Population Group: Human Expanders: Apply equivalent subjects Search modes - Boolean/Phrase Language: English; Age Groups: Childhood (birth-12 yrs), Adolbescence (13-17 yrs); Population Group: Human Expanders: Apply equivalent subjects Search modes - Boolean/Phrase Language: English; Age Groups: Childhood (birth-12 yrs), Adolbescence (13-17 yrs); Population Group: Human Expanders: Apply equivalent subjects Search modes - Boolean/Phrase Sand Search modes -				
Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Limiters - Published Date: 2012/0601 - 20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Expanders - Ap				
Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase			20201231; English;	
Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase				
S31 NOT S6				
S31 NOT S6			Childhood (birth-12	
13-17 yrs; Population Group: Human Expanders - Apply equivalent subjects Search modes - Society Search modes -				
Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Emitters - Published Date: 20120601 - 20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Expanders - Expanders - Apply equivalent subjects E				
Expanders - Apply equivalent subjects Search modes - Soolean/Phrase			Population Group:	
S32 S31 NOT S6				
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Date: 20120601- 20201231; English; Language: English; Age Groups: Childhood (brith-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase S33 S28 AND (S8 OR S10)				
20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	S32	S31 NOT S6		639
Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase				
Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase				
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(13-17 yrs); Population Group: Human Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Expanders - Apply equivalent subjects Search modes - Boolean/Phrase Expanders - Apply equivalent subjects Expanders - Apply equivalen				
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S34 S33 Limiters - Published Date: 20120601 - 20201231; English; Language: English;	S33	S28 AND (S8 OR S10)		21 608
Search modes - Boolean/Phrase		923 7 H 12 (33 31 3 10)		21,000
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Date: 20120601- 20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase S35			Boolean/Phrase	
20201231; English; Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase	S34	S33	Limiters - Published	2,063
Language: English; Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase S35 S34 NOT S6 Say Say Not S6 Say Say Not S6 Say Say Not S6 Say Not S6 Say Say Not S6 S				
Age Groups: Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase S35 S34 NOT S6 Search modes - Boolean/Phrase S36 S35 Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - Boolean/Phrase S23				
Childhood (birth-12 yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase S35 S34 NOT S6 Search modes - Boolean/Phrase S36 S35 Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523				
yrs), Adolescence (13-17 yrs); Population Group: Human Search modes - Boolean/Phrase S35 S34 NOT S6 S35 S35 Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - Boolean/Phrase S23 Search modes - Boolean/Phrase Search modes - Boolean/Phrase Search modes - Boolean/Phrase Search modes - Boolean/Phrase				
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S36 S35 Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523	605	C24 NOT CC		4 622
S36 S35 Limiters - Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523	S35	334 NOT 30		1,032
Methodology: - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - Systematic Review, META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase 2,378 Boolean/Phrase 523	636	Q35		30
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META ANALYSIS, METASYNTHESIS Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - S23				
S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523				
Search modes - Boolean/Phrase S37 S35 NOT S36 Search modes - Boolean/Phrase Sample modes - Boolean/Phrase Sample modes - Boolean/Phrase Sample modes - Boolean/Phrase Search modes - Boolean/Phrase 2,378 Search modes - Boolean/Phrase Search modes - Boolean/Phrase Search modes - Boolean/Phrase 523 Sample modes - Search modes -				
S37 S35 NOT S36 Search modes - 1,593 Boolean/Phrase Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523				
S37 S35 NOT S36 Search modes - Boolean/Phrase S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523				
S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Boolean/Phrase 2,378 Boolean/Phrase 523	S37	S35 NOT S36		1,593
S38 "Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S1 OR S18 OR S28) AND S38 Search modes - 523				, -
Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR "Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523	S38	"Pediatric Symptom Checklist-17" OR PSC OR "Revised Children's		2,378
"Strength and Difficulties Questionnaires" OR SDQ S39 (S1 OR S18 OR S28) AND S38 Search modes - 523		Anxiety and Depression Scale" OR RCADS OR RCADS-25 OR	Boolean/Phrase	•
S39 (S1 OR S18 OR S28) AND S38 Search modes - 523		"Strength and Difficulties Questionnaires" OR SDQ		
Boolean/Phrase	S39	(S1 OR S18 OR S28) AND S38		523
			Boolean/Phrase	

#	Query	Limiters/Expanders	Results
S40	\$39	Limiters - English; Language: English;	345
		Age Groups: Childhood (birth-12	
		yrs), Adolescence (13-17 yrs);	
		Population Group: Human	
		Search modes - Boolean/Phrase	
S41	S40 NOT S6	Search modes - Boolean/Phrase	281

Psychinfo

Suicide Risk: January 1, 2012, through April 30, 2020

Anxiety: NA Depression: NA

	piession. IVA				
#	Query	Limiters/Expanders	Results		
S1	(MH "Suicide+") OR TI parasuicid*OR TI "self harm"	Expanders - Apply equivalent subjects	38,801		
	OR (MH "Self-Injurious Behavior") OR TI suicid*	Search modes - Boolean/Phrase			
S2		Limiters - Published Date: 20120601- 20201231; English Language; Exclude MEDLINE records; Human; Age Groups: Infant, Newborn: birth-1 month, Infant: 1-23 months, Child, Preschool: 2-5 years, Child: 6-12 years, Adolescent: 13-18 years; Language: English Search modes - Boolean/Phrase	150,128		
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	1,855		
S4	PT Biography OR PT Cartoon OR PT Commentary OR PT Directories OR PT Editorial OR PT Games OR PT Glossary OR PT Interview OR PT Legal Case OR PT Letter OR PT Obituary OR PT Poetry OR "comment on" OR "cross-sectional" OR "retrospective cohort" OR rats OR cow OR cows OR chicken OR chickens OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murine OR murinae		1,348,371		
S5	S3 NOT S4	Search modes - Boolean/Phrase	1,507		

#	Query	Limiters/Expanders	Results
S6	(MH "Health Screening") OR TI screen OR AB	Search modes - Boolean/Phrase	212,836
	screen OR TI screening OR AB screening OR TI		
	screened OR AB screened OR TI screens OR AB		
	screens OR TI "case finding" OR AB "case finding"		
	OR TI casefinding OR AB casefinding OR "Adapted-		
	SAD PERSONS" OR "Beck Hopelessness Scale" OR		
	"Beck Scale for Suicide Ideation" OR "Center for		
	Epidemiologic Studies-Depression Scale" OR "Child		
	Suicide Assessment" OR "Columbia Suicide Severity		
	Rating Scale" OR "Columbia Teen Screen" OR		
	"Firestone Assessment of Self-Destructive Thoughts"		
	OR "Harkavy Asnis Suicide Survey" OR "Inventory		
	for Suicidal Ideation" OR "Multi-attitude Suicide		
	Tendency Scale for Adolescents" OR "Paykel Suicide		
	Items" OR "Positive and Negative Suicide Ideation		
	Inventory" OR "Scale for Suicide Ideation" OR "Self-		
	harm behavior questionnaire" OR "Suicide Behaviors		
	Questionnaire" OR "Suicidal Ideation Questionnaire"		
	OR "Suicidality Occurring in Paediatrics-Suicidality		
	Assessment Scale" OR "Suicide Assessment Five-		
	Step Evaluation and Triage" OR "Suicide Probability		
	Scale" OR TI BSI OR AB BSI OR TI CES-D OR AB		
	CES-D OR TI CSA OR AB CSA OR TI C-SSSR OR		
	AB C-SSSR OR TI CTS OR AB CTS OR TI HASS-II		
	OR AB HASS-II OR TI ISO-30 OR AB ISO-30 OR TI		
	PANSI OR AB PANSI OR TI SSI OR AB SSI OR TI		
	SHBQ OR AB SHBQ OR TI SBQ-14 OR AB SBQ-14		
	OR TI SBQ-C OR AB SBQ-C OR TI SIQ OR AB SIQ		
	OR TI SIQ-Junior OR AB SIQ-Junior OR TI STOP- SAS OR AB STOP-SAS OR TI SAFE-T OR AB		
	SAFE-T OR TI SPS OR AB SPS OR TI SRS OR AB		
	SRS		
S7	S5 AND S6	Search modes - Boolean/Phrase	163
S8	(MH "Antianxiety Agents+") OR (MH "Antidepressive	Search modes - Boolean/Phrase	71,793
	Agents+") OR (MH "Serotonin Uptake Inhibitors+")		
	OR (MH "Tranquilizing Agents+") OR TI		
	antidepressant* OR AB antidepressant* OR TI		
	antidepressives OR AB antidepressives OR TI		
	"antidepressive agents" OR AB "antidepressive		
	agents" OR TI "antidepressive drug" OR AB		
	"antidepressive drug" OR "antidepressive drugs" OR		
	"antidepressive drugs" OR "norepinephrine reuptake		
	inhibitor" OR "norepinephrine reuptake inhibitors" OR		
	"selective serotonin reuptake inhibitor" OR "selective		
	serotonin reuptake inhibitors" OR TI ssri OR AB ssri		
	OR TI ssris OR AB ssris OR "serotonin		
	norepinephrine reuptake inhibitor" OR "serotonin		
	norepinephrine reuptake inhibitors" OR snri* OR		
	"TCA antidepressants" OR "tricyclic antidepressant"		
	OR "tricyclic antidepressants" OR anafranil OR		
	celexa OR citalopram OR clomipramine OR		
	duloxetine OR escitalopram OR fluoxetine OR		
	fluvoxamine OR ketamine OR Lexapro OR lithium		
	OR luvox OR sertraline OR Zoloft		
S9	S5 AND S8	Search modes - Boolean/Phrase	44

#	Query	Limiters/Expanders	Results
S10	(MH "Behavior Therapy+") OR (MH "Cognitive Therapy+") OR (MH "Combined Modality Therapy+") OR (MH "Counseling+") OR (MH "Health Care Delivery, Integrated") OR (MH "Family Therapy") OR (MH "Patient Care/AM/MT/NU/OG/ST") OR (MH "Problem Solving+") OR (MH "Psychotherapy+") OR (MH "Psychotherapy+") OR (MH "Psychotherapy, Group+") OR (MH "Support Groups+") OR (behavior* AND (therap* or treatment* OR intervention*)) OR CBT OR (cognitive AND (therap* OR treatment* OR intervention*)) OR "care delivery" OR "care management" OR "collaborative care" OR "combination therapy" OR "combined modality" OR counsel* OR "delivery of care" OR "dialectical behavior therapy" OR "family therapy" OR "family support" OR interpersonal therap* OR interpersonal intervention* OR "means restriction" OR "means restrictions" OR "mentalization therapy" OR (parent* AND education) OR "problem solving" OR "psychoeducation" OR psychotherap* OR (risk* AND reduc*) OR "self help"	Search modes - Boolean/Phrase	777,586
S11	S5 AND S10	Search modes - Boolean/Phrase	590
S12	S9 OR S11	Search modes - Boolean/Phrase	616
S13	S12	Limiters - Publication Type: Meta Analysis, Meta Synthesis, Systematic Review Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	49
S14	S12 NOT S13	Search modes - Boolean/Phrase	567

Criteria	Include	Exclude
Condition definition	Major depressive disorder, as defined by DSM criteria (present in at least 50% of the enrolled study population)	Other mental health disorders (e.g., obsessive compulsive disorder, posttraumatic stress disorder,
	Anxiety disorders include generalized anxiety disorder, social anxiety disorder, panic disorder, agoraphobia, separation anxiety disorder, and selective mutism	psychotic disorders, bipolar disorder, cyclothymia, adjustment disorder with depressed mood), persistent depressive disorder/dysthymia,
	Definitions for increased risk of suicide may vary by study but may include suicidal ideation (suicidal thoughts or plan for suicide), history of suicide attempts (nonfatal, self-directed, and potentially injurious behavior that is intended to result in death), and deliberate self-harm	disruptive mood dysregulation disorder, premenstrual dysphoric disorder, substance/medication- induced depressive disorder, depressive disorder due to another medical condition, and depression not
	Included studies may address these conditions individually or in combination	otherwise specified; substance/medication-induced anxiety disorder, anxiety disorder due to another medical condition, and anxiety not otherwise specified
Population	 KQs 1–3: Children and adolescents (mean age ≤18 years). Studies may include: Unselected primary care population Primary care patients without known depression, anxiety disorders, or increased risk of suicide (including deliberate self-harm) Comparable community-based population 	 Adults (age ≥19 years) Studies in which more than 50% of the population are age 19 years or older Studies limited to populations that are not broadly generalizable to primary care populations (e.g.,
	KQs 4, 5: Children and adolescents (age ≤18 years) with major depressive disorder, anxiety disorders, or increased risk of suicide	populations with mental health conditions other than anxiety, depression, and increased suicide risk); persons with treatment- resistant depression or anxiety;
	A priori priority populations of interest include by age (children vs. adolescents), race/ethnicity, sex, gender identity, and sexuality	persons in residential, institutional, or inpatient settings; persons with developmental disorders (e.g., autism spectrum disorder, ADHD); persons in the midst of a suicidal crisis that are identified through their use of healthcare services related to a suicide attempt (e.g., in the emergency department); studies that require patients to have a specific clinical condition for enrollment (e.g., cancer, chronic illness, epilepsy)

Criteria	Include	Exclude
Interventions	KQs 1–3: Screening interventions with or without additional	KQs 1-3: Studies reporting on a
	provider or patient-facing elements such as referral support,	screening instrument that does not
	treatment guidelines, symptoms monitoring, and standardized	have established validity and scoring
	treatment. Screening tools must be brief standardized	mechanism or thresholds for use within
	instruments designed to identify persons with major	clinical practice
	depressive disorder, anxiety disorders, or an increased risk of	
	suicide; self-report with or without parental report, clinician	KQs 4, 5 (all disorders): Other
	administered, or electronically delivered (<5 minutes if clinician	treatment modalities (e.g., exercise,
	administered, <15 minutes if self-administered) instruments	light therapy, transcranial magnetic
	are eligible	nerve stimulation, electroshock
		treatment, diet and herbal supplements
	KQs 4, 5 (depression and suicide):	such as St. John's wort and other
	Counseling (e.g., psychotherapy, psychoeducation, suicide	complementary and alternative
	means restriction)	medicine, social marketing, policy,
	Care delivery models targeting improved mental health	system-level interventions, or
	outcomes (e.g., collaborative care, care management)	adjunctive agents to enhance the
	Pharmacotherapy agents approved for pediatric use (e.g.,	effects of antidepressants)
	duloxetine, fluoxetine, escitalopram, sertraline,	Interventions involving components
	fluvoxamine), generally first-line	that could not be replicated in most
	Include combination therapies	healthcare settings, including
		environmental components (media
	KQs 4, 5 (anxiety):	messages, public signage),
	 Cognitive behavioral therapy (including exposure therapy)* 	interventions on groups in closed
	Include eligible psychotherapy studies regardless of mode	(preexisting) social networks (e.g., in
	of intervention	daycares, schools), or those requiring
	Pharmacotherapy agents approved for pediatric use (e.g.,	the parent to have the target condition
	clonidine, duloxetine, fluoxetine, escitalopram, sertraline,	
	fluvoxamine), generally first-line	Pharmacotherapeutic agents that are
	Include combination therapies	not FDA approved for pediatric use
		(e.g., paroxetine, vortioxetine)
		100 1.5 1. 1. 1. 1. 1. 1. 1. 1.
		KQs 4, 5 (anxiety): Psychotherapy
Camana = = = 1 = = = =	KOo 4 2 (correspinal). Hereal core/on correspina	other than cognitive behavioral therapy
Comparators	KQs 1, 3 (screening): Usual care/no screening	KQs 1, 3: No comparator
	KQ 2 (depression and anxiety): Clinical diagnosis based on	KQ 2: Another screening instrument,
	structured clinical interview by qualified professional using	non-standardized clinical diagnosis
	standard diagnostic criteria in place at the time of the study	(i.e., diagnosis not made based on
	(e.g., DSM-IV or DSM-5)	existing <i>DSM</i> criteria at the time of the
	(Sig., 25% 17 0) 25% 0)	study)
	KQ 2 (suicide): Assessment of increased suicide risk based	
	on clinical interview by qualified professional	KQs 4, 5: No comparator, active
	, , , , , , , , , , , , , , , , , , , ,	intervention (i.e., comparative
	KQs 4, 5 (psychotherapy and care delivery):	effectiveness) (e.g., medication X vs.
	No intervention	medication Y would not be eligible.
	Wait-list control (i.e., delayed treatment)	CBT plus medication X vs. CBT plus
	Attention control (i.e., receives interpersonal interaction	medication Y would not be eligible)
	but no other elements of the active intervention)	
	Usual care (e.g., referral to treatment, non-standardized)	KQ 4, 5 (anxiety and depression):
	treatment, or unclear treatment services)	Treatment as usual comparator groups
		where the comparator group receives
	KQs 4, 5 (suicide risk only): Treatment as usual (the	standard treatment services that
	provision of standard treatment services not governed by a	involve a reasonably standardized
	study protocol, but at a duration and level of intensity	active intervention provided outside of
	consistent with active treatment interventions) are also eligible	a study protocol are not eligible
	KQs 4, 5 (pharmacotherapy): Placebo (including placebo	
	along with psychotherapy, when compared with the active	
	agent plus the same psychotherapy intervention (e.g., CBT	
	plus placebo vs. CBT plus medication would be eligible)	

Criteria	Include	Exclude
Outcomes	 KQs 1, 4: Depression or anxiety symptoms, remission or diagnosis, or response Suicide deaths, suicide attempts and deliberate self-harm, or suicidal ideation All-cause mortality Quality of life measured using validated scales or instruments Functioning (using validated scales or instruments, days of missed school) KQ 2: Sensitivity, specificity, or data to calculate one or both Negative predictive value, positive predictive value, area under the curve/ area under the receiver operating characteristic/receiver operating characteristic, diagnostic odds/likelihood ratios, Youden's index KQ 3: False alarm False reassurance KQs 3, 5: Treatment avoidance Deterioration in patient-provider relationship Labeling or stigma Inappropriate/unnecessary treatment KQ 5 (pharmacotherapy only): Serious adverse effects Withdrawals due to adverse effects Suicidality 	All KQs: All other outcomes
Outcome assessment timing Setting	No minimum followup KQs 1–3: Recruitment of participants from: Primary care settings (e.g., pediatrics, family medicine, or school-based health clinics) Virtual or community settings such as schools, if population comparable to general primary care (i.e., focus on "healthy" children or adolescents, or broad spectrum of medical and mental health conditions in rates comparable to primary care setting)† General emergency departments KQs 4, 5: Treatment in: Primary care or specialty clinics, including school-based health clinics Virtual or community-based settings General EDs are eligible for recruitment of patients to an intervention; however, interventions delivered solely/entirely within an ED setting are not eligible	KQ 1: Studies conducting school-wide or community-wide screening are not eligible. KQs 1–3: Referred or established patients at mental health clinics Inpatient/residential facilities Correctional facilities Psychiatric emergency departments KQs 4, 5: Treatment in: Correctional facilities Schools involving school-wide interventions Inpatient/residential facilities Psychiatric emergency departments

Criteria	Include	Exclude
Study design	KQs 1, 3: RCTs, CCTs	All other study designs
	KQ 2: Studies of diagnostic test accuracy [‡]	KQ 2: Psychometric development and internal (e.g., split sample) validation
	KQ 3: RCTs, CCTs, observational studies	studies of new instruments; case- control studies (i.e., designs that limit
	KQ 4: RCTs	the study sample to only those with and without known mental health
	KQ 5:	symptoms)
	• RCTs	
	 Systematic reviews of comparative cohort and case-control observational studies 	KQs 1–4: Systematic reviews of RCTs (reviews will only be used to identify
	 Harms of pharmacotherapy only: large (>1,000 participants) comparative cohort and case-control observational studies published after identified systematic reviews that include observational studies 	relevant studies)
Study geography	Primary studies that primarily take place in countries categorized as "Very High" on the 2019 Human Development	Reviews in which >50% of included studies take place in countries not
	Index (as defined by the United Nations Development	categorized as "Very High" on the
	Programme)	Human Development Index
Publication language	English	Any language other than English
Quality rating	Fair- or good-quality studies	Poor-quality studies

^{*} We summarized the effect of other non-CBT interventions for anxiety as a contextual question, using a best-evidence approach. † We intended to restrict inclusion of school-based recruitment to studies conducting the screening in other settings (e.g., mental health clinics) but on review of studies, elected to include all studies using a school-based recruitment because of the difficulty of ascertaining the location of screening in some studies.

Abbreviations: ADHD=attention deficit hyperactivity disorder; AUC=area under the curve; AUROC=area under the receiver operating characteristic; CBT=cognitive behavioral therapy; CCT=controlled, clinical trial; DSM=Diagnostic and Statistical Manual of Mental Disorders; ED=emergency department; FDA=U.S. Food and Drug Administration; KQ=key question; NPV=negative predictive value; PPV=positive predictive value; RCT=randomized, controlled trial; ROC=receiver operating characteristic.

[†] We cataloged all studies reporting on instruments that otherwise meet all eligibility criteria, but our synthesis will focus on the instruments that are reported in more than one study.

Randomized, Controlled Trials and Cohort Studies

Criteria

- Initial assembly of comparable groups
- Randomized, controlled trials (RCTs)—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, crossovers, adherence, and contamination)
- Important differential loss to followup or overall high loss to followup
- Measurements that are equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: Adjustment for potential confounders for cohort studies or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

Definition of Ratings Based on Above Criteria

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (followup ≥80%); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention is given to confounders in analysis. In addition, intention-to-treat analysis is used for RCTs.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially, but some question remains on whether some (although not major) differences occurred in followup; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for. Intention-to-treat analysis is lacking for RCTs.

Poor: Studies will be graded "poor" if any of the following major limitations exist: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied equally among groups (including not masking outcome assessment); and key confounders are given little or no attention. Intention-to-treat analysis is lacking for RCTs.

Sources: U.S. Preventive Services Task Force. U.S. Preventive Services Task Force, Procedure Manual, Appendix VI. Rockville, MD: U.S. Preventive Services Task Force, 2015;⁶¹ Harris et al, 2001.⁶²

Systematic Reviews

Criteria

- Comprehensiveness of sources considered/search strategy used
- Standard appraisal of included studies
- Validity of conclusions
- Recency and relevance (especially important for systematic reviews)

Definition of Ratings Based on Above Criteria

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions

Fair: Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies

Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies

Sources: U.S. Preventive Services Task Force. U.S. Preventive Services Task Force, Procedure Manual, Appendix VI. Rockville, MD: U.S. Preventive Services Task Force, 2015;⁶¹ Harris et al, 2001.⁶²

Appendix D Table 1. Individual Study Quality Assessment of Harms of Screening Studies Based on Cochrane RoB 2.0 (KQ 3)

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Harms	Harms Comments
Gould et al,	Some concerns	Low	Low	Low	Some concerns	Some concerns	Method of randomization not
2005 ⁶³							reported, minimal baseline
							characteristics reported to assess
							adequacy of randomization; no trial
							registration or study protocol cited to
							determine whether analysis
							conducted was prespecified.
Robinson et	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	No baseline characteristics provided
al, 2011 ⁶⁴							to assess adequacy of
							randomization; between 20% and
							40% of students had missing data
							and unclear how missing data are
							related to outcome of distress; no
							trial registration or evidence of a
							prespecified analysis plan.

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Arendt et al.	Low	Some	Low	Low	Low	Some	No blinding possible.	Not	
2016 ⁶⁵		concerns				concerns	31	Applicable	
Asarnow et al, 2017 ⁶⁶	Low	Low	Some concerns	Low	Some concerns	Some concerns	Some differential attrition but reasonable sensitivity analyses conducted to demonstrate likely not a major	Not Applicable	
							concern; pilot study without clearly specified primary outcome or timepoint with multiple analyses conducted.		
Asbrand et al, 2020 ⁶⁷	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns	Wait-list control so participants and interventionists were not masked and PROs were used.	Applicable	
Atkinson et al, 2014 ⁶⁸	Low	Low	High	Low	Low	High	High and differential attrition.	J	High and differential attrition
Baer et al, 2005 ⁶⁹	High	High	Low	High	Low	High		Not Applicable	
Barrett et al, 1996 ⁷⁰	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns	Potential for bias from attrition.	Not Applicable	
Barrett et al, 1998 ⁷¹	Some concerns	High	Low	Low	Low	High		Not Applicable	
Beidel et al, 2007 ⁷²	Some concerns	High	High	High	Low	High		Not Applicable	
2003 ⁷³	Some concerns	Some concerns	Some concerns	Some concerns	Low	Some concerns	Differential attrition for side effects (disinhibition), potentially risking effective unmasking during outcome assessment, but the study notes that participants and staff had the same rate of accurate guesses of treatment across all arms.	Some concerns	
Black et al, 1994 ⁷⁴	Some concerns	Low	Low	Some concerns	Low	Some concerns		Not Applicable	
Brent et al, 1997 ⁴⁹	Some concerns	High	High	High	Low	High	No patient or provider blinding, unknown outcome assessor blinding, high attrition, several in the study should have been ineligible.	J	High and possibly differential attrition, unblinded outcome assessors, participants and clinicians not blinded

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Clarke et al, 2016 ⁷⁵	Some concerns	Some concerns	Low	Low	Low	Some concerns	Patient and provider not blinded; patients, parents, and clinical personnel awareness of treatment could influence outcomes.	Some concerns	
Clarke et al, 2005 ⁷⁶	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns	No allocation concealment and patients and providers not blinded.	Applicable	
Clarke et al, 1999 ⁴⁵	Some concerns	Some concerns	High	Some concerns	Low	Some concerns	Randomization and allocation concealment not reported; patients not blinded, awareness of intervention could influence outcomes; high attrition and unknown differential attrition.	Not Applicable	Moderate attrition, no details on randomization or allocation concealment or blinding, awareness of intervention could influence outcomes
Cobham et al, 2017 ⁷⁷	Some concerns	Low	Low	Low	Low	Some concerns		Not Applicable	
Cobham et al, 2012 ⁷⁸	High	Some concerns	Low	Low	Some concerns	High	No allocation concealment.	Not Applicable	
Cornacchio et al, 2019 ⁷⁹	Low	Some concerns	Low	Low	Low	Some concerns	Participants and therapists aware of treatment status.	Not Applicable	
Cottrell et al, 2018 ⁸⁰	Low	Low	Low	Low	Low	Low		Not Applicable	
Diamond et al, 200281	Some concerns	Some concerns	Low	Some concerns	High	High	Awareness of intervention could influence outcomes.	High	
Diamond et al, 2010 ⁸²	Low	Low	Low	Some concerns	Low	Some concerns	Outcome assessors not masked but administered PROs, not clinical interviews. Masking of intervention to patients and caregivers not feasible.	Not Applicable	
Donovan et al, 2014 ⁸³	Low	Some concerns	High	Low	Low	Some concerns	Some concerns for all outcomes other than PAS, high ROB for PAS.	Not Applicable	
Ehrenreich- May et al, 2017 ⁸⁴	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns	No information about randomization or allocation concealment; masking of participants and outcome assessment of PROs not feasible and wait-list control	Not Applicable	

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
							group, no prespecified analysis plan.		
Emslie et al, 2014 ⁸⁵	Low	Low	Some concerns	Low	Low	High	High and differential attrition.	High	High and differential attrition
Emslie et al, 2009 ⁸⁶	Some concerns	Low	Low	Low	Low	Some concerns	Awareness of the intervention could influence outcomes. No allocation concealment and patients and providers not blinded.	Not Applicable	
Emslie et al, 2002 ⁸⁷	Some concerns	Low	High	Low	Low	High	High and differential attrition with LOCF for ITT without further investigation, no sensitivity analysis. Possible imbalance at baseline.	Not Applicable	
Emslie et al, 1997 ⁸⁸	Some concerns	Low	High	Some concerns	Low	High	High and differential attrition.	High	High and differential attrition
Flannery- Schroeder et al, 2000 ⁸⁹	Some concerns	High	Low	High	Low	High		Not Applicable	
Fristad et al, 201990	Low	Some concerns	Low	Low	Low	Some concerns	Therapy not masked.	Low	
Gallagher et al, 200491	Some concerns	High	Some concerns	High	Low	High		Not Applicable	
Ginsburg et al, 2020 ⁹²	Low	Low	Some concerns	Low	Some concerns	Some concerns	Nearly a quarter of data was missing at post treatment for some measures, imputed; no prespecified analysis plan.	Not Applicable	
Green et al, 2011 ⁹³	Low	Low	Low	Low	Low	Low	Masking of intervention to participants and caregivers not feasible.	Not Applicable	
Griffiths et al, 2019 ⁹⁴	Low	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns for ED presentation for self-harm outcome; high concerns for all other outcomes because of >50% missing data at post treatment and beyond.	High	5 AEs reported but no description of the events, only that they weren't related to the study. Also not reported by group.
Hancock et al, 201841	Low	Some concerns	High	Low	Low	High	Differential attrition that likely influenced the results.	Not Applicable	
Hazell et al, 2009 ⁹⁵	Low	Low	Low	Low	Low	Low	Masking of intervention to patients and caregivers not feasible.	Not Applicable	

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Hetrick et al, 2017 ⁹⁶	Low	Low	High	Low	Low	High	High concerns from differential and high attrition with no analysis of impact of missing data.	Not Applicable	
Hill et al, 2019 ⁹⁷	Low	Low	Low	Low	Some concerns	Low		Not Applicable	
Hirshfeld- Becker et al, 2010 ⁹⁸	Low	Some concerns	Some concerns	Low	Low	Some concerns		Not Applicable	
Holmes et al, 2014 ⁹⁹	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns		Not Applicable	
Hooven et al, 2012 ¹⁰⁰	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	No information about randomization, allocation concealment and minimal information about baseline characteristics; masking of caregivers not feasible and mostly PROs used, unclear whether some measures used are valid and reliable; attrition not reported by group; no prespecified analysis plan.	High	
Infantino et al, 2016 ¹⁰¹	Some concerns	High	Low	High	Low	High		Not Applicable	
Ingul et al, 2014 ¹⁰²	Low	Low	High	Low	Low	High	High attrition.	Not Applicable	
Ishikawa et al, 2019 ¹⁰³	Low	Some concerns	Low	Low	Low	Some concerns	Some concerns due to fact that assignment to treatment is not masked.	Not	
Kendall et al, 1997 ¹⁰⁴	Some concerns	High	High	High	Low	High		Not Applicable	
Kendall et al, 1994 ¹⁰⁵	Some concerns	High	Some concerns	High	Low	High		Not Applicable	
Khanna et al, 2010 ¹⁰⁶	High	High	Low	High	Low	High		Not Applicable	
King et al, 2015 ¹⁰⁷	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns because method of randomization not reported, unclear whether allocation concealment was adequate, minimal baseline characteristics presented to judge adequacy of	Not Applicable	

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
							randomization, no prespecified analysis plan.		
King et al, 2009 ¹⁰⁸	Low	Low	Some concerns	Low	Low	Some concerns	Modest attrition, unclear masking of participants and interventionists.	Not Applicable	
Last et al, 1998 ¹⁰⁹	Some concerns	High	High	High	Low	High		Not Applicable	
Lau et al, 2010 ¹¹⁰	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns		Not Applicable	
Luby et al, 2018 ¹¹¹	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns	Wait-list control prevented masking of participants and interventionists and PROs used; no prespecified analysis plan.	Not Applicable	
Lyneham et al, 2006 ¹¹²	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns		Not Applicable	
	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns	High attrition, unclear allocation status, no patient blinding in some groups.	Some concerns	High attrition but no differential attrition, no specified outcome blinding or patient/intervention provider blinding reported.
March et al, 2009 ¹¹⁴	Some concerns	High	Low	High	Low	High		Not Applicable	
Mehlum et al, 2014 ¹¹⁵	Low	Low	Low	Low	Low	Low		Not Applicable	
Melfsen et al, 2011 ¹¹⁶	Some concerns	High	High	High	Low	High		Not Applicable	
Mufson et al, 1999 ¹¹⁷	Some concerns	Some concerns	High	Low	Low	High	Not blinded, high attrition, very large differential attrition.	High	High and differential attrition, awareness of intervention could influence outcomes
Mufson et al, 2004 ¹¹⁸	Low	Low	Low	Low	Some concerns	Some concerns	No prespecified analysis plan.	Not Applicable	
Nauta et al, 2003 ¹¹⁹	High	Some concerns	Low	Some concerns	Some concerns	High	Did not follow an accepted strategy for randomization and allocation concealment, excluded some participants from being assigned to wait-list condition and baseline imbalances between the two	Not Applicable	

	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall RoB			
Author, Year	RoB	RoB	RoB	RoB	RoB	Efficacy	Efficacy Comments	Harms RoB	Harms Comments
							active treatment groups, masking not feasible and use of PROs, no information about whether clinical outcome assessors were masked, no		
Öst et al, 2015 ¹²⁰	Low	Low	Some concerns	Some concerns	Low	Some concerns	prespecified analysis plan.	Not Applicable	
Ougrin et al, 2013 ¹²¹	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns	Masking of clinicians not feasible, allocation concealment not possible and unclear whether clinicians were involved in recruitment; long term outcomes not part of original trial analysis plan.	Not Applicable	
Perrin et al, 2019 ¹²²	Low	Low	Low	Some concerns	Low	Some concerns		Not Applicable	
2010123	High	Some concerns	Low	Some concerns	Some concerns	High	Potential for randomization issues.	Not Applicable	
Pine et al, 2001 ¹²⁴	Some concerns	Low	Some concerns	Low	Low	Some concerns	Potential for attrition bias.	Some concerns	
Pineda et al, 2013 ¹²⁵	Low	Some concerns	Low	Low	Low	Some concerns	Masking not feasible.	Not Applicable	
Rapee et al, 2006 ¹²⁶	Some concerns	High	High	High	Low	High		Not Applicable	
Richardson et al, 2014 ¹²⁷		Low	Low	Low	Low	Low		Low	
1999 ⁴⁴	Some concerns	Some concerns	High	High	Some concerns	High	No ITT analyses conducted; randomization method not reported; blinding of assessors not reported; no group differences reported at baseline other than for outcomes so do not know how groups may have differed on sociodemographic characteristics, etc., and analyses were not adjusted. High and differential attrition.	Not Applicable	
Rossouw et al, 2012 ¹²⁸	Low	Some concerns	Low	Low	Low	Some concerns	Treatment not masked (not feasible).	Some concerns	Treatment not masked (not feasible).

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Rudy et al, 2017 ¹²⁹	Some concerns	Low	Low	Low	Some concerns	Some concerns	No information about method of randomization and allocation concealment and some imbalances at baseline that may be due to small sample size; no prespecified analysis plan.	Not Applicable	Trainis Comments
Rynn et al, 2001 ¹³⁰	Some concerns	Low	Low	Low	Low	Some concerns		Not Applicable	
Salzer et al, 2018 ⁴²	Low	Some concerns	Some concerns	Low	Low	Some concerns	High attrition and inability to blind participants or therapists.	Low	
Sánchez- García et al, 2009 ¹³¹	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns	Insufficient information to rate most domains.	Not Applicable	
Santucci et al, 2013 ¹³²	Low	High	Low	High	Some concerns	High		Not Applicable	
Schneider et al, 2011 ¹³³	Some concerns	High	Low	High	Low	High		Not Applicable	
Pineda et al, 2013 ¹²⁵	Low	Some concerns	Low	Low	Low	Some concerns	Masking not feasible.	Not Applicable	
Rapee et al, 2006 ¹²⁶	Some concerns	High	High	High	Low	High		Not Applicable	
Richardson et al, 2014 ¹²⁷	Low	Low	Low	Low	Low	Low		Low	
Rossello et al, 1999 ⁴⁴	Some concerns	Some concerns	High	High	Some concerns	High	No ITT analyses conducted; randomization method not reported; blinding of assessors not reported; no group differences reported at baseline other than for outcomes so do not know how groups may have differed on sociodemographic characteristics, etc., and analyses were not adjusted. High and differential attrition.	Not Applicable	
Rossouw et al, 2012 ¹²⁸	LOW	Some concerns	Low	Low	Low	Some concerns	Treatment not masked (not feasible).	Some concerns	Treatment not masked (not feasible).
Rudy et al, 2017 ¹²⁹	Some concerns	Low	Low	Low	Some concerns	Some concerns	No information about method of randomization and allocation concealment and	Not Applicable	

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
ramor, roa							some imbalances at baseline that may be due to small sample size; no prespecified analysis plan.		
Rynn et al, 2001 ¹³⁰	Some concerns	Low	Low	Low	Low	Some concerns		Not Applicable	
Salzer et al, 2018 ⁴²	Low	Some concerns	Some concerns	Low	Low	Some concerns	High attrition and inability to blind participants or therapists.	Low	
Sánchez- García et al, 2009 ¹³¹	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns	Insufficient information to rate most domains.	Not Applicable	
Santucci et al, 2013 ¹³²	Low	High	Low	High	Some concerns	High		Not Applicable	
Schneider et al, 2011 ¹³³	Some concerns	High	Low	High	Low	High		Not Applicable	
Rynn et al, 2001 ¹³⁰	Some concerns	Low	Low	Low	Low	Some concerns		Not Applicable	
Salzer et al, 2018 ⁴²	Low	Some concerns	Some concerns	Low	Low	Some concerns	High attrition and inability to blind participants or therapists.	Low	
Sánchez- García et al, 2009 ¹³¹	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns	Insufficient information to rate most domains.	Not Applicable	
Santucci et al, 2013 ¹³²	Low	High	Low	High	Some concerns	High		Not Applicable	
Schneider et al, 2011 ¹³³	Some concerns	High	Low	High	Low	High		Not Applicable	
Shortt et al, 2001 ¹³⁴	Some concerns	Low	Low	Some concerns	Low	Some concerns	No information on randomization and blinding of outcome assessors.	Some concerns	
Silverman et al, 1999 ¹³⁵	Some concerns	Some concerns	High	Low	Low	High	Potential for attrition bias.	Not Applicable	
Smith et al, 2014 ¹³⁶	Some concerns	Some concerns	High	Low	Low	High	Potential for attrition bias.	Not Applicable	
Spence et al, 2017 ¹³⁷	Some concerns	High	Some concerns	High	Some concerns	High		Not Applicable	
Spence et al, 2006 ¹³⁸	Some concerns	High	Low	High	Low	High		Not Applicable	
Spence et al, 2000 ¹³⁹	Low	High	Low	High	Low	High		Not Applicable	
Spence et al, 2011 ¹⁴⁰	Some concerns	High	High	High	Low	High		Not Applicable	

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Stjerneklar et al, 2019 ¹⁴¹	Low	Some concerns	Low	Low	Low	Some concerns	Wait list control and no masking. Nothing reported on masking of assessors. However, in the discussion it does say that the masking of assessors was broken.	Not Applicable	Trainis Comments
Strawn et al, 2015 ¹⁴²	Low	Low	Some concerns	Low	Low	Some concerns	77% attrition, ITT analyses performed.	Some concerns	
Strawn et al, 2020 ¹⁴³	Low	Low	Some concerns	Low	Low	Some concerns		Low	
Tang et al, 2009 ¹⁴⁴	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns	Methods of randomization and allocation concealment not reported, no information about how many participants were analyzed or missing data; no prespecified analysis plan.	Not Applicable	
Thirlwall et al, 2013 ¹⁴⁵	Low	Some concerns	Some concerns	Low	Low	Some concerns	Differential attrition, but sensitivity analyses suggest no difference.		
Tillfors et al, 2011 ¹⁴⁶	Some concerns	Some concerns	High	Some concerns	Low	High	Potential for differential attrition, lack of information on randomization, allocation concealment, and blinding.	Not Applicable	
Topooco et al, 2018 ¹⁴⁷	Some concerns	Low	Low	Some concerns	Low	Some concerns	Risk of bias of outcome measurements showed some concern.	Low	
Topooco et al, 2019 ¹⁴⁸	Low	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns for assignment to intervention and some concerns for measurement of outcome.	Low	
Vigerland et al, 2016 ¹⁴⁹	Some concerns	High	Low	High	Low	High		Not Applicable	
Villabø et al, 2018 ¹⁵⁰	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns	assignment; no information regarding whether trial analyzed in accordance with prespecified plan; no information about trial registry.	Not Applicable	
Wagner et al, 2006 ¹⁵¹	Some concerns	Some concerns	High	Some concerns	Low	Some concerns	High attrition but no differential attrition, no specified outcome blinding or patient/intervention provider blinding reported.	Some concerns	High overall attrition.

Author, Year	Domain 1 RoB	Domain 2 RoB	Domain 3 RoB	Domain 4 RoB	Domain 5 RoB	Overall RoB Efficacy	Efficacy Comments	Harms RoB	Harms Comments
Waite et al,	Some	Some	Some	Some	Low	Some	Wait-list and no masking and	Low	
2019152	concerns	concerns	concerns	concerns		concerns	missing data.		
Walkup et al, 2008 ¹⁵³	Low	Some concerns	Low	Low	Low	Some concerns	Participants assigned to combined sertraline and CBT were aware of their sertraline assignment.	Concerns	Participants assigned to combined sertraline and CBT were aware of their sertraline assignment
Warner et al, 2011 ¹⁵⁴	Some concerns	High	Low	High	Low	High		Not Applicable	
Waters et al, 2009 ¹⁵⁵	Some concerns	Some concerns	High	Low	Low	High		Not Applicable	
Weersing et al, 2017 ¹⁵⁶	Some concerns	Some concerns	Some concerns	Some concerns	Low	Some concerns	Masking of intervention not feasible. Potential for bias from differential attrition and issues with blinding in outcome assessment.	Not Applicable	
Weihs et al, 2018 ¹⁵⁷	Some concerns	Low	Some concerns	Some concerns	Low	High	Unclear methods of randomization and allocation concealment, how ITT was done, whether outcome assessors were blinded.	concerns	Unclear methods of randomization and allocation concealment, how ITT was done, whether outcome assessors were blinded.
Wergeland et al, 2014 ¹⁵⁸	Some concerns	High	Low	High	Low	High	Potential for bias in randomization and outcome assessment.	Not Applicable	
Wood et al, 2001 ¹⁵⁹	Low	Low	Low	Low	Low	Low	No information on missing data or how it was handled.	Not Applicable	
Wuthrich et al, 2012 ¹⁶⁰	Some concerns	High	Low	High	Low	High	LOGE LA L	Not Applicable	L DAG D. L. I

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; ED=emergency department; ITT=intent to treat; LOCF=last observation carried forward; PAS=Preschool Anxiety Scale; PRO=patient-reported outcome; ROB\RoB=risk of bias.

Appendix D Table 3. Individual Study Quality Assessment of Meta-Analysis on the Risk of Bias Assessment Tool for Systematic Reviews (ROBIS)

		Identification and Selection of Studies	Data Collection and Study Appraisal		
Author Year	Study Eligibility Concern	Concern	Concern	Synthesis and Findings Concern	Risk of Bias
Cipriani et al, 2016 ¹⁶¹	Low	Low	Low	Low	Low

Abbreviations: ROBIS=Risk of Bias Assessment Tool for Systematic Reviews.

Appendix D Table 4. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 1

Author Year	Did the study adequately describe methods of patient selection?	Did the study describe the index test and describe how it was conducted and interpreted?	Did the study describe the reference standard and how it was conducted and interpreted?	Did the study describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table?	Did the study describe included patients (prior testing, presentation, use of index test and setting)?	
Bailey et al, 2006 ²¹	Yes	Yes	Yes	Yes	• • •	No
Canals et al, 2001 ¹⁷	Yes	Yes		No	Yes	Yes
Canals et al, 2012 ¹⁶²	Yes	Yes	Yes	Yes	Yes	Yes
Christensen et al, 2015 ¹⁵	Yes	Yes	Yes	Yes	Yes	Yes
Cunha et al, 2008 ¹⁶³	Yes	Yes	Yes	Yes	Yes	Unclear
Garcia-Lopez et al, 2015 ¹⁶⁴	Yes	Yes	Yes	Yes	Yes	No
Gardner et al, 2007 ¹⁶⁵	Yes	Yes	Yes	Unclear	Yes	Yes
Hopper et al, 2012 ¹⁶⁶	Yes	Yes	Yes	Yes		No
Johnson et al, 2002 ¹³	Yes	Yes	Yes	Yes	Yes	Yes
Johnson et al, 2006167	Yes	Yes	Yes	No	Yes	Yes
Katon et al, 2008 ¹⁶⁸	Yes	Yes	Yes	Yes	Yes	Yes
Muris et al, 2001 ¹⁶⁹	Yes	Yes	Yes	No	Yes	Yes
O'Connor et al, 2016 ¹⁴	Yes	Yes	Yes	No	Yes	Yes
Patton et al, 1999 ¹⁹	Yes	Yes	Yes	No	Yes	No
Queen et al, 2012 ²³	Yes	Yes	Yes	Yes	Yes	Yes
Ranta et al, 2007 ¹⁷⁰	Yes	Yes	Yes	Unclear	Yes	Yes
Ranta et al, 2012 ¹⁷¹	Yes	Yes	Yes	Yes	Yes	Yes
Rivera-Riquelme et al, 2019 ¹⁷²	Yes	Yes	Unclear	Unclear	Yes	Yes
Roberts et al, 1991 ¹⁶	Yes	Yes	Yes	Yes	Yes	Yes
Thompson et al, 1999 ²⁴	Yes	Yes	Yes	No	Yes	No
Tsai et al, 2009 ¹⁷³	Yes	Yes	Yes	Yes	Yes	Yes
Patton et al, 1999 ¹⁹	Yes	Yes	Yes	No	Yes	Yes

Appendix D Table 5. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 2

Author Year	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge of the results of the reference standard?	Is the reference standard likely to correctly classify the target condition?	Was there an appropriate interval between index test(s) and reference standard?	design avoided?	If a threshold was used, was it prespecified?
Bailey et al, 2006 ²¹	Yes	Unclear	Yes	Unclear	Yes	No
Canals et al, 2001 ¹⁷	Yes	Yes	Yes	Yes	Yes	No
Canals et al, 2012 ¹⁶²	No	Yes	Yes	Yes	Unclear	Yes
Christensen et al, 2015 ¹⁵	Yes	Yes	Yes	Yes		No
Cunha et al, 2008 ¹⁶³	Unclear	Yes	Yes	Unclear		No
Garcia-Lopez et al, 2015 ¹⁶⁴	No	Unclear	Yes	Unclear	Yes	No
Gardner et al, 2007 ¹⁶⁵	No	Yes	Yes	Yes	Yes	Yes
Hopper et al, 2012 ¹⁶⁶	Yes	Yes	Yes	Unclear	Yes	No
Johnson et al, 2002 ¹³	Yes	No	Yes	Yes	Yes	No
Johnson et al, 2006 ¹⁶⁷	Yes	Unclear	Unclear	Yes	Yes	Yes
Katon et al, 2008 ¹⁶⁸	Yes	Yes	Yes	Yes	Yes	Yes
Muris et al, 2001 ¹⁶⁹	No	Unclear	Yes	Yes	Yes	Yes
O'Connor et al, 2016 ¹⁴	Yes	No	Unclear	Yes	Yes	No
Patton et al, 1999 ¹⁹	Yes	Yes	Yes	Unclear	Yes	Unclear
Queen et al, 2012 ²³	Yes	Unclear	Yes	Yes	Yes	No
Ranta et al, 2007 ¹⁷⁰	Yes	Yes	Yes	Yes	Yes	Yes
Ranta et al, 2012 ¹⁷¹	Yes	Unclear	Yes	Yes	Yes	Yes
Rivera-Riquelme et al, 2019 ¹⁷²	Yes	Yes	Yes	Yes	Yes	Yes
Roberts et al, 1991 ¹⁶	Unclear	Yes	Yes	Unclear	Yes	No
Thompson et al, 1999 ²⁴	Yes	Yes	Yes	Unclear	Yes	Unclear
Tsai et al, 2009 ¹⁷³	Yes	Unclear	Yes	Yes	Yes	Unclear
Patton et al, 1999 ¹⁹	Yes	Yes	Unclear	Yes	Yes	Unclear

Appendix D Table 6. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 3

Author Year	Were the reference standard results interpreted without knowledge of the results of the index test?	Did all patients receive a reference standard?	Did the study avoid inappropriate exclusions?	Did all patients receive the same reference standard?	Were all patients included in the analysis?
Bailey et al, 2006 ²¹	Unclear	Yes	Yes	Yes	Yes
Canals et al, 2001 ¹⁷	Yes	No	Yes	Yes	No
Canals et al, 2012 ¹⁶²	Yes	Yes	Unclear	Yes	Yes
Christensen et al, 2015 ¹⁵	Yes	Yes	Yes	Yes	Unclear
Cunha et al, 2008 ¹⁶³	Yes	Yes	No	Yes	Yes
Garcia-Lopez et al, 2015 ¹⁶⁴	Unclear	Yes	Yes	Yes	Yes
Gardner et al, 2007 ¹⁶⁵	Yes	No	No	Yes	No
Hopper et al, 2012166	Yes	No	Yes	Yes	No
Johnson et al, 2002 ¹³	No	Yes	Yes	Yes	No
Johnson et al, 2006167	No	No	Yes	No	No
Katon et al, 2008 ¹⁶⁸	Yes	Yes	Yes	Yes	No
Muris et al, 2001 ¹⁶⁹	Unclear	Yes	No	Yes	Yes
O'Connor et al, 2016 ¹⁴	No	Yes	Yes	Yes	Yes
Patton et al, 1999 ¹⁹	Unclear	No	Yes	Yes	No
Queen et al, 2012 ²³	Unclear	Yes	Yes	Yes	Yes
Ranta et al, 2007 ¹⁷⁰	Yes	No	Yes	Yes	No
Ranta et al, 2012 ¹⁷¹	Unclear	Yes	Yes	Yes	Yes
Rivera-Riquelme et al, 2019 ¹⁷²	Yes	No	Yes	Yes	No
Roberts et al, 1991 ¹⁶	Yes	Yes	Yes	Yes	Yes
Thompson et al, 1999 ²⁴	Unclear	No	Yes	Yes	No
Tsai et al, 2009 ¹⁷³	Unclear	Yes	Yes	Yes	Yes
Patton et al, 1999 ¹⁹	Unclear	Yes	Yes	Yes	No

Appendix D Table 7. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool, Part 4

Author Year			Could the reference standard, its conduct, or interpretation have introduced bias?	Could the patient flow have introduced bias?	Are there concerns that the included patients do not match the review question?
Bailey et al, 2006 ²¹	Unclear	Unclear	Unclear	Unclear	Unclear
Canals et al, 2001 ¹⁷	No	Unclear	_	No	No
Canals et al, 2012 ¹⁶²	Yes	No	No	No	Yes
Christensen et al, 2015 ¹⁵	No	Unclear	No	No	No
Cunha et al, 2008 ¹⁶³	Yes	Unclear	No	Unclear	Unclear
Garcia-Lopez et al, 2015 ¹⁶⁴	Unclear	Unclear	Unclear	Unclear	No
Gardner et al, 2007 ¹⁶⁵	Yes	No	No	Yes	Yes
Hopper et al, 2012 ¹⁶⁶	No	Unclear	No	Unclear	No
Johnson et al, 200213	Unclear	Yes	Yes	Yes	No
Johnson et al, 2006 ¹⁶⁷	No	Unclear	Yes	Yes	No
Katon et al, 2008 ¹⁶⁸	No	No	No	Unclear	No
Muris et al, 2001 ¹⁶⁹	Yes	Unclear	Unclear	No	No
O'Connor et al, 2016 ¹⁴	No	Yes	Yes	No	Unclear
Patton et al, 1999 ¹⁹	No	Unclear	Unclear	Unclear	No
Queen et al, 2012 ²³	Unclear	Yes	Unclear	No	No
Ranta et al, 2007 ¹⁷⁰	No	No	No	Unclear	No
Ranta et al, 2012 ¹⁷¹	No	Unclear	Unclear	No	No
Rivera-Riquelme et al, 2019 ¹⁷²	No	No	No	Unclear	No
Roberts et al, 1991 ¹⁶	Unclear	Unclear	No	Unclear	No
Thompson et al, 1999 ²⁴	No	Unclear	Unclear	Unclear	No
Tsai et al, 2009 ¹⁷³	No	Unclear	Unclear	Unclear	Yes
Patton et al, 1999 ¹⁹	No	Unclear	Unclear	No	No

Appendix D Table 8. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 5

Author Year	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	Overall Study Quality	Rationale for Overall Rating
Bailey et al, 2006 ²¹	No	No	Fair	Only 99 participants (from the 1,470 that were randomly selected to participate) completed the full study so applicability uncertain. Blinding of index test and reference test results not reported, interval between testing NR, index test thresholds not prespecified.
Canals et al, 2001 ¹⁷		No	Fair	Thresholds for index test were not prespecified.
Canals et al, 2012 ¹⁶²	No	No	Fair	Spectrum bias possible given the way the sample was selected (high and low scorers on the SCARED instrument administered the prior year).
Christensen et al, 2015 ¹⁵	No	No	Fair	Index test thresholds not prespecified.
Cunha et al, 2008 ¹⁶³	No	No	Poor	Selection into this analysis based on results of prior tests/evaluations as part of a larger study, participants with and without diagnoses were selected, this analysis excluded all participants with a diagnosis of ADHD or other mood disorder, index test thresholds not prespecified, interval between index and reference test not specified.
Garcia-Lopez et al, 2015 ¹⁶⁴	No	No	Fair	Sample assembled based on scoring above a threshold on index test and then a random sample of those who scored below threshold; blinding of index test and referent tests not reported, interval of administration between index and reference test not reported, thresholds not prespecified.
Gardner et al, 2007 ¹⁶⁵	No	No	Poor	Sample was derived from a separate study that screened persons for entry into a study of anxiety and abdominal pain and mood disorders and mental health service use; thus, only children who screened positive on the SMFQ or SCARED were included thus high likelihood of spectrum bias. Children who did not screen positive did not receive a reference test, so sensitivity and specificity in an unselected primary care population cannot be determined.
Hopper et al, 2012 ¹⁶⁶	No	No	Fair	Index threshold not specified; interval between index and reference test NR; only a sample of the entire screened population received a reference test, but the sample selected appears to represent the spectrum of scores.

Appendix D Table 8. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 5

Author Year	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	Overall Study Quality	Rationale for Overall Rating
Johnson et al, 2002 ¹³	No	No	Poor	Only a small proportion of those eligible actually participated in the study so although recruitment was consecutive, potential for selection bias. Several thresholds evaluated for index text, unclear timing between index screening test and clinical interview. Interviewers not masked to results of index text. Of 373 who agreed to participate, only 294 were included (78.9%), and no information is provided on those who were missing from the sample. The information on the index and reference standard were collected by the same interviewer during the telephone call, so the interviewer had knowledge of the index test and reference standard results.
Johnson et al, 2006 ¹⁶⁷	No	No	Poor	Only patients who had a positive screen received a clinical interview to confirm risk for suicide.
Katon et al, 2008 ¹⁶⁸	No	No	Fair	Participants with an interval between index and reference test of more than 18 days were excluded from the analysis.
Muris et al, 2001 ¹⁶⁹	No	No	Fair	Inappropriate exclusions of patients for the analysis; recruitment methods NR; whether results of index and reference tests were masked was NR.
O'Connor et al, 2016 ¹⁴	No	No	Poor	Same interviewer administered the index test and reference standard so results not masked, thresholds for index test not prespecified, unclear that lay administers of reference standard with high school degree and 12 hours of training is equivalent to a clinician interview and diagnosis. Study specifically recruited children with asthma in addition to healthy children, so applicability to general population is uncertain.
Patton et al, 1999 ¹⁹	No	No	Fair	Index test threshold seems to have been based on normative data; unclear whether reference test interviewers were blinded to the index test results; unclear interval between index and reference test; only a sample of participants from the full sample were selected to receive the reference test and unclear how that sample was selected; however, it appears the sample did include participants from the low and high spectrum of scores.
Queen et al, 2012 ²³	No	No	Fair	Thresholds for index test were not prespecified, unclear whether results of index and referent test were blinded, sample was enriched with some persons from specialty mental health settings.

Appendix D Table 8. Individual Study Quality Assessment of Diagnostic Accuracy Studies Based on the QUADAS-2 Tool Part 5

Author Year	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	Overall Study Quality	Rationale for Overall Rating
Ranta et al, 2007 ¹⁷⁰	No	No	Fair	Not all screened persons received the reference test; all those who screened positive received reference test plus 2 participants who screened negative were selected randomly for the reference test for each person that screened positive.
Ranta et al, 2012 ¹⁷¹	No	No	Fair	Blinding of index and reference test not reported, index test thresholds not prespecified.
Rivera-Riquelme et al, 2019 ¹⁷²	No	No	Fair	Only a sample of participants matched on sex scoring in the low and medium score ranges received the reference standard and were included in the analysis.
Roberts et al, 1991 ¹⁶	No	No	Fair	Selection based on initial screening test scores, included all subjects above a prespecified threshold, and a random selection of participants from below the threshold; index test thresholds not prespecified, interval between index and reference test up to a month.
Thompson et al, 1999 ²⁴	Unclear	Unclear	Fair	Unclear threshold for MHI index test; interval between index and reference standard not specified; only a random sample of all persons screened received diagnostic reference standard.
Tsai et al, 2009 ¹⁷³	No	No	Fair	Index test did not have prespecified thresholds used, unclear whether index test was blinded to results of reference test.
Patton et al, 1999 ¹⁹	Unclear	No	Fair	Unclear whether SRS thresholds for the risk group was established a priori, unclear whether interviewers were blinded to results of the SRS; two possible reference standards used (direct suicide risk, clinical risk assessment); SRS was embedded in larger survey so unclear how its validity may be different if used as a stand-alone instrument.

Abbreviations: ADHD=attention deficit hyperactivity disorder; MHI=Mental Health Index; NR=not reported; QUADAS-2=Quality Assessment of Diagnostic Accuracy Studies; SCARED=Screen for Anxiety Related Emotional Disorders; SMFQ=Short Mood and Feelings Questionnaire; SRS=Suicide Risk Screen.

Instrument	Full Name	Description	Scoring, Range	Studies Using Instrument
ANS ¹⁷⁴	Autonomic Nervous System Questionnaire	in the past 6 months the respondent has ever had a sudden spell or an attack of feeling frightened, anxious, or very uneasy and/or a spell or an attack with the heart racing, feeling faint, or an inability to catch one's breath. A "no" response to both questions is considered a negative screen. Items 3–5 for those who answered yes to one or two of the first questions ask about spontaneity, frequency, and anticipatory worry about panic attacks.	Each item on a 3-point scale (not at all worried, somewhat worried, or very worried). The total score range is 0 to 5.	Queen et al, 2012 ²³
BDI ¹⁷⁵	Beck Depression Inventory		mild to moderate depression, 19 to 29	Canals et al, 2001; ¹⁷ Roberts et al, 1991 ¹⁶
CES-D ^{18, 176-178}	Center for Epidemiologic Studies-Depression	A 20-item self- or interviewer-administered scale that assess past-week symptoms. Respondents asked to indicate frequency of past-week symptoms as "rarely or none of the time" (scored as 0), "some or a little of the time" (scored as 1), "occasionally or a moderate amount of time" (scored as 2), and "most or all of the time" (scored as 3). A version modified for children is referred to as the CES-DC.	Scores range from 0 to 60. Higher scores indicate worse symptoms; a score of 16 or higher is considered positive for depression.	Garrison et al, 1991 ¹⁸ Roberts et al, 1991 ¹⁶
CIS-R ¹⁷⁹	Clinical Interview Schedule Revised	populations. It includes 14 subscales specific to the	A screen is positive if it fulfills the algorithm for ICD-10 depressive disorder.	Patton et al, 1999 ¹⁹
EDAS ¹⁸⁰	Escala para la Deteccion de Ansiedad Socia	A 26-item youth report that measures social anxiety. Items assess fear of speaking or acting in ways that would be embarrassing, youths' social avoidance, distress, and interference. Administration time is 16 minutes.	Two items are dichotomous, and the remaining items are on a 5-point scale (0 to 4). The nondichotomous items are summed for the total score ranging from 24 to 120.	Garcia-Lopez et al, 2015 ¹⁶⁴

Instrument	Full Name	Description	Scoring, Range	Studies Using Instrument
HSCL ^{181, 182}	Hopkins Symptom Checklist	A 10- or 6-item depression subscale derived from the Symptom Checklist-90. Items asking about troublesome feelings with responses scored as no (1), slightly (2), much (3), and very much (4).	Score ranges from 10 to 40 for the 10-item version. A score of 16 was considered the optimal threshold for screening in the initial validation study.	Christensen et al, 2015 ¹⁵
LSAS-CA ¹⁸³	The Liebowitz Social Anxiety Scale for Children and Adolescents	A youth-reported 24-item scale to measure social anxiety appropriate for children and adolescents. The screener assesses total fear, fear of social interaction, fear of performance, total avoidance, avoidance of social interaction, and performance avoidance. Administration time is 12 minutes.	The screener uses a 4-point Likert scale (0 to 3). Total scores range from 0 to 72.	Garcia-Lopez et al, 2015 ¹⁶⁴
MHI-5	Mental Health Index	The MHI-5 is a 5-item version of the 38-item MHI. The 5 items pertain to mood in the past month.	Originally designed as a 6-point Likert scale, modified to 4-point Likert scale. Total scores range from 0 to 15. Higher scores indicate better mental health.	Rivera-Riquera et al, 2018 ¹⁷²
PHQ-A ¹⁸⁴	Patient Health Questionnaire- Adolescents	Derived from the original PRIME-MD screening questionnaire and clinical interview; PHQ-A is a 67-item self-administered questionnaire that can be administered in 5 minutes or less to assess anxiety and depressive disorders. Clinicians quickly review completed questionnaires and apply diagnostic algorithms, which appear at the bottom of the printed page. The instrument is used to screen for panic disorder and GAD among other psychiatric disorders including depression and substance use.	NR	Johnson et al, 2002 ¹³
PI-ED	Paediatric Index of Emotional Distress – Total Scale; Anxiety Subscale; Depression Subscale	A brief, self-report screening tool based on HADS to measure 16 anxiety and depression symptoms that is suitable for children and adolescents ages 8 to 16 years. Items are scored on a 4-point scale from 3 to 0 (always, a lot of the time, sometimes, not at all). Includes a total score, an anxiety subscale, and a depression subscale.	Items are scored on a 4-point scale, 0 to 3 from "always" to "not at all." Total score ranges from 0 to 21.	O'Connor et al, 2016 ¹⁴

Instrument	Full Name	Description	Scoring, Range	Studies Using Instrument
SCARED ¹⁸⁵⁻¹⁸⁷	Screen for Anxiety Related Emotional Disorders	41-Item parent and child self-report measure used to screen for anxiety disorders in children ages 8 to 18 years. A total score is available as well as for the following scales: GAD, separation anxiety disorder, panic disorder, and social anxiety disorder. Administration time is 10 minutes. A 10-item short form is also available.	Each item is rated on a 3-point scale ranging from 0 to 2 ("almost never," "sometimes," "often"). Score ranges from 0 to 82. Total score >25 may indicate anxiety disorder; subscale scores also available (panic: score of 7 or more; GAD: score of 9 or more; social anxiety: score of 8 or more; separation anxiety: score of 5 or more).	Bailey et al, 2006 ²¹ Canals et al, 2012 ¹⁶² Muris et al, 2001 ¹⁶⁹
SAS ^{188, 189}	Social Anxiety Scale	An 18-item screener plus four filler items used to assess social anxiety in children in relation to peers. It includes three scales: Fear of Negative Evaluation, Social Avoidance and Distress-Specific to New Peers and New Situations, and General Social Avoidance and Distress. Includes both a child and adult report version. The SAS for Adolescents (SAS-A) is a revision of the SAS to make it developmentally appropriate for adolescents. SAS-A includes 18 items and same three scales with both an adolescent and parent version.	Each item on a 5-point scale ("not at all" to "all the time"). Total score ranges from 18 to 90.	Bailey et al, 2006 ²¹ Garcia-Lopez et al, 2015 ¹⁶⁴
SASA ¹⁹⁰	Social Anxiety Scale for Adolescents (Slovenian measure)	28-item instrument measuring social anxiety with two scales: one measuring fears, worries, and anticipation of a negative peer evaluation and the second assessing social tension/relaxation, speech or behavior inhibition, and readiness to exposure in social situations. Administration time is 12 minutes.	scale. The total score ranges from 28 to 140.	Garcia-Lopez et al, 2015 ¹⁶⁴
SoPhI ¹⁹¹	Social Phobia Inventory	A 21-item scale to assess social anxiety using DSM-IV criteria, including an item assessing duration of symptoms (social anxiety must be present for at least 6 months). Administration time is 10 minutes.	All items are rated on a 5- point scale, with the total score ranging from 21 to 105.	Garcia-Lopez et al, 2015 ¹⁶⁴
SPAI-B ¹⁹²	Social Phobia and Anxiety Inventory - Brief	16-item scale measuring social anxiety in adolescents. The screener assesses cognitive, somatic, and behavioral symptoms. Administration time is 9 minutes.		Garcia-Lopez et al, 2015 ¹⁶⁴

Instrument	Full Name	Description	Scoring, Range	Studies Using Instrument
	Social Phobia	17 items measuring behavioral, physiological, and	Each item is rated on a 5-	Garcia-Lopez et al, 2015 ¹⁶⁴
Mini-SPIN ^{194, 195}	Inventory/Mini Social	cognitive symptomatology associated with social	point 0 to 4 scale ("not at	Ranta et al, 2007 ¹⁷⁰
	Phobia Inventory	anxiety; fear in social situations; avoidance of	all" to "extremely"), with a	Ranta et al, 2012 ¹⁷¹
		performing in social situations; and physiological	total score ranging from 0	Tsai et al, 2009 ¹⁷³
		discomfort in social situations. Time to administer is 8	to 68 for the full	
		minutes. The MiniSPIN is a 3-item version of the scale	instrument and from 0 to	
		measuring avoidance and fear of embarrassment.	12 for the Mini SPIN.	
SWQ ¹⁹⁶	Social Worries	10-Item parent-report screener to assess social	Each item on a 3-point	Bailey et al, 2006 ²¹
	Questionnaire	anxiety symptomatology in youth ages 8 to 17 years. It	scale (not true to mostly	-
		measures the degree to which the youth avoids or	true). Total scores range	
		worries about particular social situations.	from 0 to 20.	
WHO-5 ^{197, 198}		A 5-item scale asking about feelings in the past 2	This scale is generally	Christensen et al, 2015 ¹⁵
			converted to a scale of 0	
		Short-Form 36 (SF-36). Response categories are all of		
	Index	the time (5), most of the time (4), more than half of the	the sum score by 4.	
		time (3), less than half of the time (2), some of the time	Higher scores represent	
		(1), and at no time (0).	more well-being.	

Abbreviations: ANS=Autonomic Nervous System Questionnaire; BDI=Beck Depression Inventory; CES=Center for Epidemiological Studies; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; EDAS=escala para la deteccion de ansiedad socia; GAD=generalized anxiety disorder; HADS=Hospital Anxiety and Depression Scale; HSCL13=Hopkins Symptom Checklist-13; ICD-10=International Classification of Diseases, Tenth Revision; KQ=key question; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; MHI=Mental Health Index; MiniSPIN=Mini-Social Phobia Inventory; NR=not reported; PHQ-A=Patient Health Questionnaire-Adolescent; PI-ED=Pediatric Index of Emotional Distress; PRIME-MD=Primary Care Evaluation of Mental Disorders; SAS=Social Anxiety Scale; SAS-A=Social Anxiety Scale for Adolescents; SCARED=Screen for Anxiety Related Emotional Disorders; SF-36=Short Form (36) Health Survey; WHO-5=World Health Organization Five Item Well-being Index.

Appendix E Table 2. Reference Standard Instruments for Anxiety Test Accuracy Studies (KQ 2)

Reference Measure	Description	Studies Using Reference Measure
Anxiety Disorders Interview	A semi-structured interview designed to diagnosis anxiety disorders as well as	Bailey et al, 2006;21 Garcia-Lopez et al,
Schedule for DSM: Child and	depression and behavioral disorders based on DSM criteria for children and	2015;164 Queen et al, 2012;23 Rivera-
Parent Version (ADIS C/P)	adolescents.	Riquelme et al, 2019 ¹⁷²
Composite International Diagnostic Interview (CIDI)	A comprehensive, structured interview designed to be used by trained lay interviewers for the assessment of mental disorders according to the definitions and criteria of ICD-10 and DSM.	Christensen et al, 2015; ¹⁵ Patton et al, 1999 ¹⁹
Computerized Diagnostic Schedule for Children (C-DISC)	14 time = 5 m	O'Connor et al, 2016 ¹⁴
Diagnostic clinical interview	Diagnostic clinical interview with mental health professional that includes items from the Structured Clinical Interview for DSM-III-R, PRIME-MD Clinical Evaluation Guide, and DSM-IV Global Assessment of Functioning.	Johnson et al, 2002 ¹³
Measure of Adolescent Potential for Suicide (MAPS) Clinical Interview	Includes direct suicide ratings (DSR) recorded during the interview, which are determined by the frequency and intrusiveness of suicidal thoughts, levels of suicide plans/preparation/intent, lethality of prior attempts, and present vs. past suicide threat. Ratings on each domain range from 0 (not at all or low lethality) to 6 (very serious or high lethality) with overall score the average of 4 ratings. High suicide risk defined as the upper 20th percentile cut-point of the DSR.	Thompson et al, 1999 ²⁴
Mini-Neuropsychiatric Interview for Kids (MINI-Kid)	A structured diagnostic interview for children and adolescents based on DSM and ICD- 10 criteria that is used to diagnose 23 Axis 1 disorders.	Canals et al, 2012;162 Tsai et al, 2009173
Schedule for affective Disorders and Schizophrenia for School-Age Children- Present and Lifetime Version (K-SADs-PL)	A semi-structured clinical interview that covers 32 DSM child and adolescent diagnoses including both MDD and anxiety disorders such as panic disorder, SepAD, SocAD, and GAD.	
Schedules for Clinical Assessment in Neuropsychiatry (SCAN)	A semi-structured diagnostic interview aligned to ICD-10 and DSM criteria.	Canals et al, 2001; ¹⁷
Structured Clinical Interview for DSM-IV for Children (K-SCID)	K-SCID for DSM-IV generates DSM-IV diagnoses on children, with probe questions to facilitate assessing whether diagnostic criteria are met.	Muris et al, 2001 ¹⁶⁹

Abbreviations: ADIS=Anxiety Disorders Interview Schedule; C-DISC=Computerized Diagnostic Schedule for Children; CIDI=Composite International Diagnostic Interview; DSM=Diagnostic and Statistical Manual of Mental Disorders; DSR=direct suicide ratings; GAD=generalized anxiety disorder; ICD-10=International Classification of Diseases, Tenth Revision; KQ=key question; K-SAD=Schedule for Affective Disorders and Schizophrenia for School-Age Children; MAPS=Measure of Adolescent Potential for Suicide; MDD=major depressive disorder; MINI-Kid=MINI international neuropsychiatric interview for kids; PRIME-MD=Primary Care Evaluation of Mental Disorders; SepAD=separation anxiety disorder; SocAD=social anxiety disorder.

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Number of Events (%)	Placebo N	Number of Events (%)	Between- Group P Value
Family CBT	Asarnow et al, 2017 ⁶⁶	15	12 weeks	Percentage with SA	3 months	20	0 (0)	22	4 (18)	0.01
	Asarnow et al, 2017 ⁶⁶	15	12 weeks	NSSI	3 months	20	Probabilities of survival without (SE) 0.55 (0.11)	22	Probabilities of survival without (SE) 0.43 (0.14)	0.054
Family Therapy	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰		6-7 sessions over 6 months	Self-harm events per participant	36 months	415	Mean (SD) 1.0 (2.19)	417	Mean (SD) 1.2 (3.22)	NR
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰		6-7 sessions over 6 months	SASII self- harm event	12 to 18 months	415	202 (75)	417	147 (70)	NR
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰		6-7 sessions over 6 months	Hospital attendance for self-harm event	12 months	415	NR	417	NR	0.56
Group psycho- therapy	Green et al, 201193	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	Frequency of self-harm	0-6 months	181	Frequency 4.6	181	Frequency 4.4	0.91
	Green et al, 201193	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	Mild severity of self-harm	6-12 months	178	68 (38)	180	76 (42)	NS
	Green et al, 201193	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better		6-12 months	178	24 (13)	180	21 (12)	NS

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Number of Events (%)	Placebo N	Number of Events (%)	Between- Group P Value
	Green et al, 201193	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	by boosters until participants felt better	Severity of self-harm	6-12 months	178	11(6)	180	13 (7)	NS
	Green et al, 201193	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	Self-harm resulting in injury	6-12 months	180	1 (0.05)	180	2 (1.1)	NR
Group MBT	Griffiths et al, 201994	16	12 sessions over 12 weeks	Self-Harm subscale (RTSHI)	12 weeks	22	Mean (SD) 26.00 (12.57)	26	Mean (SD) 12 (12.28)	NS
	Griffiths et al, 201994		12 sessions over 12 weeks			22	Mean (SD) 38.78 (19.65)	26	Mean (SD) 36.00 (18.80)	NS
	Griffiths et al, 201994	16	12 sessions over 12 weeks	Self-harm ED presentation	12 weeks	22	Mean (range) 0.36 (0 to 2)	26	Mean (range) 0.23 (0 to 2)	NS
Group therapy	Hazell et al, 2009 ⁹⁵	14	12 months	Engaged in repetition of self-harm	8 weeks	34	30 (88)	34	24 (71)	0.07
Develop- mental Group Therapy	Wood et al, 2001 ¹⁵⁹	14	Median of 8 group sessions and 2.5 indiviual sessions over 6 months	Number of episodes of deliberate self-harm	7 months	32	Mean (95% CI) 0.6 (0.3 to 0.9)	31	Mean (95% CI) 1.8 (0.6 to 3.0)	NR
	Wood et al, 2001 ¹⁵⁹	14	Median of 8 group sessions and 2.5 indiviual sessions over 6 months	Number of persons repeating self-harm	7 months	32	2 (6)	31	10 (32)	OR, 6.3 (1.4 to 28.7)

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	N	Number of Events (%)	Placebo N	(%)	Between- Group P Value
Individual and Family DBT	Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³	16	1 weekly individual session, 1 weekly multifamily skills training, and family sessions and telephone coaching outside of sessions as needed, over 19 weeks	Self-harm episode	19 weeks		Mean (95% CI) 9.0 (4.8 to 13.2)	38	Mean (95% CI) 22.5 (11.4 to 33.5)	0.05
	Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³	16	1 weekly individual session, 1 weekly multifamily skills training, and family sessions and telephone coaching outside of sessions as needed, over 19 weeks	Admitted to hospital due to self-harm	19 weeks	39	1 (2)	38	2 (5)	NS
	Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³	16		ER visit due to self-harm	19 weeks	39	2 (5)	38	5 (13)	NS
Therapeutic assessment	Ougrin et al, 2013 ¹²¹ Ougrin, 2011 ²⁰⁴	16	1 session	One or more presentation to A&E with self-harm	2 years	35	7 (20)	34	9 (26)	0.53

Treatment		Mean Age	Dose and	Outcome	Time Point		Number of	Placebo		Between- Group P
(Condition)	Author, Year	(Years)	Duration	Measure	(Weeks)	N	Events (%)	N	(%)	Value
Individual and family MBT	Rossouw et al, 2012 ¹²⁸	15	Weekly sessions over 12 months	Self-harm (RTSHI)	12 months	40	Log mean (SE) 1.33 (0.22)		Log mean (SE) 2.01 (0.21)	<0.01
	Rossouw et al, 2012 ¹²⁸	15		At least one incident of self-harm	12 months	40	22 (56)	40	33 (83)	0.01
Youth- nominated support team	King et al, 2009 ¹⁰⁸	16		Suicide attempt	12 months	175	29 (17)	171	35 (20)	0.51

Abbreviations: A&E=accident and emergency; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; DBT=dialectical behavioral therapy; ED=emergency department; ER=emergency room; IG=intervention group; MBT=mentalization-based therapy; N=number; NR=not reported; NS=not significant; NSSI=non-suicidal self-injury; OR=odds ratio; RTSHI=Risk-Taking and Self-Harm Inventory for Adolescents; SA=suicide attempt; SASII=Suicide Attempt Self-Injury Interview; SD=standard deviation; SE=standard error.

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Family CBT	Asarnow et al, 2017 ⁶⁶	15	12 weeks	Percent with suicide attempts		20	NR		NR	NA	NA
Family Therapy	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	14	over 6 months	BSS	12 months	415	0.26 (0.05)	417	0.36 (0.05)	OR (95% CI): 0.64 (0.44 to 0.94)	0.024
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	14	6-7 sessions over 6 months	HSFC	12 months	415	4.8 (0.40)		5.1 (0.43)	Mean difference: -0.3 (-1.1 to 0.4)	0.38
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	14	6-7 sessions over 6 months	CDRS-R	12 months	248	33.2(1.46)	189	33.9(1.57)	Mean difference: -0.6 (-3.1 to 1.9)	0.62
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	14	6-7 sessions over 6 months	PQ-LES	12 months	415	49.9 (1.12)	417	48.8 (1.13)	Mean difference: 1.1 (-0.5 to 2.7)	0.18
	Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	14	6-7 sessions over 6 months	GHQ	12 months	415	12.8 (0.61)	417	13.5 (0.65)	Mean difference: -0.7 (-1.8 to 0.3)	0.19
Attachment- Based Family Therapy	Diamond et al, 2010 ⁸²	15	5 to 8 sessions over 12 weeks	SIQ-Jr	12 weeks	35	5.2 (1.6-8.8)	31	16.2 (10.1- 22.2)	NR	NR
	Diamond et al, 2010 ⁸²	15	5 to 8 sessions over 12 weeks	SSI	12 weeks	35	69.2 (50.2- 88.2)	31	34.6 (15.0- 54.2)	NR	NR
	Diamond et al, 2010 ⁸²	15	5 to 8 sessions over 12 weeks	BDI-II	12 weeks	35	12.6 (8.0- 17.2)	31	18.5 (12.9- 24.0)	NR	NR
Group psychotherapy	Green et al, 2011 ⁹³	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	SIQ	6 months	171	61.5 (45.5)	9	59.9 (48.4)	0.07 (-8.60 to 8.75)	0.99

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group psychotherapy (continued)	Green et al, 2011 ⁹³	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	MFQ	6 months	171	28.5 (16.1)		27.6 (16.5)	-0.44 (-3.49 to 2.61)	0.78
	Green et al, 2011 ⁹³	12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62)	6 weeks followed by boosters until participants felt better	HoNOSCA	6 months	172	12.2 (6.3)	180	12.6(6.1)	-0.55 (-1.64 to 0.54)	0.32
Group MBT	Griffiths et al, 201994	16	12 sessions over 12 weeks	RCADS MD	12 weeks	22	20.39 (4.74)	26	18.15 (6.57)		NS
Group therapy	Hazell et al, 200995	14	6+ sessions over 12 months	SIQ	8 weeks	34	74.11 (41.75)	37	76.40 (54.28)		p=0.80
	Hazell et al, 200995	14	6+ sessions over 12 months	MFQ	8 weeks	34	30.91 (17.25)	37	32.38 (19.94)		p=0.60
	Hazell et al, 200995	14	6+ sessions over 12 months	CGAS	8 weeks	25	58.54 (8.70)	25	60.59 (10.69)		
	Hazell et al, 200995	14	6+ sessions over 12 months	HoNOSCA	8 weeks	26	16.77 (7.12)	29	15.00 (9.28)		
	Hazell et al, 200995	14	6+ sessions over 12 months	SDQ	8 weeks	33	17.66 (6.58)	37	18.89 (7.16)		
Developmental Group Therapy	Wood et al, 2001 ¹⁵⁹	14	Median of 8 group sessions and 2.5 indiviual sessions over 6 months	SIQ	7 months	28	47.3 (50.5)	27	39.7 (46.7)	7.5 (-18.8 to 33.9)	

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo N	(SD/SE)	Between- Group Difference	Between- Group P Value
Developmental Group Therapy (continued)	Wood et al, 2001 ¹⁵⁹	14	group sessions and 2.5 indiviual sessions over 6 months			29		27	15.3 (13.0)	3.5 (-4.4 to 11.3)	
	Wood et al, 2001 ¹⁵⁹	14	Median of 8 group sessions and 2.5 indiviual sessions over 6 months	HoNOSCA	7 months	31	8.4 (6.4)	31	6.9 (6.1)	1.5 (-1.7 to 4.7)	NR
Individual internet CBT	Hill et al, 2019 ⁹⁷	17	2 sessions 1 week apart	BSS	2 weeks	41	2.05 (3.27)	39	4.49 (6.01)		0.12
	Hill et al, 201997	17	2 sessions 1 week apart	RADS-2	2 weeks	41	23.12 (4.50)	39	24.64 (5.90)		0.45
Interpersonal psychotherapy	Tang et al, 2009 ¹⁴⁴	15		BHS	6 weeks	35	7.74 (5.29)	38	12.42 (4.08)		P<0.01
	Tang et al, 2009 ¹⁴⁴	15	2 weekly sessions and weekly phone call, over 6 weeks	BSS	6 weeks	35	8.97 (10.77)	38	16.29 (7.99)		P<0.01
	Tang et al, 2009 ¹⁴⁴	15	2 weekly sessions and weekly phone call, over 6 weeks	BDI-II	6 weeks	35	19.97 (14.68)	38	31.58 (12.01)		P<0.001

Treatment		Mean Age	Dose and	Outcome	Time Point	Treatment	Treatment Score	Placebo	Placebo Score	Between-	Between- Group P
(Condition)	Author, Year	(Years)	Duration	Measure	(Weeks)	N	(SD/SE)	N	(SD/SE)	Group Difference	Value
Individual and	Mehlum et al, 2014 ¹¹⁵	16	1 weekly	SIQ-Jr			20.45	37		Between-	0.110
Family DBT	Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰²		individual session, 1				(19.15)			group difference	
	Haga et al, 2018 ²⁰³		weekly							in slope:	
	riaga et al, 2010		multifamily							0.15	
			skills training,								
			and family								
			sessions and								
			telephone								
			coaching								
			outside of								
			sessions as								
			needed, over 19 weeks								
	Mehlum et al, 2014 ¹¹⁵	16	1 weekly	BHS	19 weeks	39	6.23 (5.30)	38	9.06 (6.53)	Between-	0.071
	Mehlum et al, 2016 ²⁰¹		individual	5.10	To Wooks		0.20 (0.00)		0.00 (0.00)	group	0.07
	Mehlum et al, 2019 ²⁰²		session, 1							difference	
	Haga et al, 2018 ²⁰³		weekly							in slope:	
	-		multifamily							-0.13	
			skills training,								
			and family								
			sessions and								
			telephone coaching								
			outside of								
			sessions as								
			needed, over								
			19 weeks								

					Time		Treatment		Placebo	Between-	Between-
Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Point (Weeks)	Treatment N	Score (SD/SE)	Placebo N	Score (SD/SE)	Group Difference	Group P Value
Individual and Family DBT (continued)		16	1 weekly individual session, 1 weekly multifamily skills training, and family sessions and telephone coaching outside of sessions as needed, over	SMFQ	19 weeks	39	10.19 (5.04)		12.58 (6.62)		0.179
	Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³	16	19 weeks 1 weekly individual session, 1 weekly multifamily skills training, and family sessions and telephone coaching outside of sessions as needed, over 19 weeks	MADRS	19 weeks	39	12.29 (7.52)	38	15.76 (8.14)	-0.22	P=0.019

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	(SD/SE)	Between- Group Difference	Between- Group P Value
Individual and Family DBT (continued)	Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³	16	1 weekly individual session, 1 weekly multifamily skills training, and family sessions and telephone coaching outside of sessions as needed, over 19 weeks	CGAS	71 weeks	38	65.68 (11.81)	37	64.22 (14.13)	Between- group difference in slope: 0.03	0.067
Individual and family MBT	Rossouw et al, 2012 ¹²⁸	15	Weekly sessions over 12 months	MFQ	12 months	40	9.26 (1.27)	40	11.54 (1.14)		P<0.05
Motivational interviewing	King et al, 2015 ¹⁰⁷	18	1 session	SIQ-Jr	2 months	24	21.46 (17.4)	22	24.28 (17.3)		NS
	King et al, 2015 ¹⁰⁷	18	1 session	BHS	2 months	24	5.66 (5.2)	22	8.64 (5.7)		NS
	King et al, 2015 ¹⁰⁷	18	1 session	RADS-2-SF		24	25.38 (4.7)	22	30.87 (4.0)		P<0.01
Therapeutic assessment	Ougrin et al, 2013 ¹²¹ Ougrin, 2011 ²⁰⁴	16	1 session			35	,	35	, ,		
	Ougrin et al, 2013 ¹²¹ Ougrin, 2011 ²⁰⁴	16	1 session	CGAS	3 months	35	64.6 (12.9)	35	60.1 (9.9)	4.49 (-0.98 to 9.96)	NR
Youth- Nominated Support Team	King et al, 2009 ¹⁰⁸	16	1 session and weeky telephone contact, 1 session and phone contact over flexible time period	BHS	6 weeks	NR	6.82 (NR)	NR	7.80 (NR)		0.09

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	(SD/SE)	Between- Group Difference	Between- Group P Value
Youth- Nominated Support Team (continued)	King et al, 2009 ¹⁰⁸	16	1 session and weeky telephone contact, 1 session and phone contact over flexible time period	SIQ-Jr	6 weeks	NR	25.55 (NR)	NR	29.71 (NR)		0.04
	King et al, 2009 ¹⁰⁸	16	1 session and weeky telephone contact, 1 session and phone contact over flexible time period	CDRS-R	6 weeks	NR	39.6 (NR)	NR	40.80 (NR)		0.40
	King et al, 2009 ¹⁰⁸	16	1 session and weeky telephone contact, 1 session and phone contact over flexible time period	CAFAS	3 months	168	15.20 (NR)	174	15.77 (NR)		0.58
RAP-P	Pineda et al, 2013 ¹²⁵	15	4 sessions over 4 to 8 weeks	ASQ-R,	Post- treatment	22	8.73 (4.88)	18	11.89 (5.47)		p=0.05
	Pineda et al, 2013 ¹²⁵	15	4 sessions over 4 to 8 weeks	HoNOSCA	Post- treatment	22	13.45 (5.89)	18	17.61 (5.20)		p<0.01

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Promoting Care, Assess, Respond, Empower	Hooven et al, 2012 ¹⁰⁰	16	C-Care, 1 session, 2 hours total	Suicide Ideation	1 month	153 155 164	IG1 Rate of change: -1.131	143	-0.917	NA	G1 and G2 vs. CG: NS
Empower			P-CARE, 2 sessions, 2 hours total				IG2 Rate of change: -1.033				G3 vs. CG: P<0.001
			C-Care plus P-CARE, 1 child session, 2 hours total; 2 parent sessions, 2				IG2 Rate of change: -1.451				
	Hooven et al, 2012 ¹⁰⁰	16	hours total C-Care, 1 session, 2 hours total P-CARE, 2 sessions, 2 hours total	Direct Suicide Threat	1 month	153 155 164	IG1 Rate of change: -0.443 IG2 Rate of change: -0.294	143	-0.318		G1 and G2 vs. CG: NS G3 vs. CG: P<0.05
			C-Care plus P-CARE, 1 child session, 2 hours total; 2 parent sessions, 2 hours total				IG2 Rate of change: -0.556				

Treatment		Mean Age	Dose and	Outcome	Time Point	Treatment	Treatment Score	Placebo	Placebo Score	Between- Group	Between- Group P
(Condition)	Author, Year	(Years)	Duration	Measure	(Weeks)	N	(SD/SE)	N	(SD/SE)	Difference	
Promoting	Hooven et al, 2012 ¹⁰⁰	16	C-Care, 1	CES-D	1 month	153	-0.951	143	-0.685	NA	P<0.01
Care, Assess,			session, 2								
Respond,			hours total								
Empower			D CADE O								
(continued)			P-CARE, 2								
			sessions, 2								
			hours total								
			C-Care plus								
			P-CARE, 1								
			child session,								
			2 hours total;								
			2 parent								
			sessions, 2								
			hours total								
	Hooven et al, 2012 ¹⁰⁰	16	C-Care, 1	CES-D	1 month	155	-0.815	143	-0.685	NA	NS
			session, 2								
			hours total								
			P-CARE, 2								
			sessions, 2								
			hours total								
			C-Care plus								
			P-CARE, 1								
			child session,								
			2 hours total;								
			2 parent								
			sessions, 2								
			hours total	1							

			_		Time		Treatment		Placebo	Between-	Between-
Treatment (Condition)	Author, Year	Mean Age (Years)	Dose and	Outcome	Point (Weeks)	Treatment	Score (SD/SE)	Placebo	Score (SD/SE)	Group Difference	Group P Value
			Duration	Measure		N		N			
Promoting	Hooven et al, 2012 ¹⁰⁰	16	C-Care, 1	CES-D	1 month	164	-1.021	143	-0.685	NA	P<0.01
Care, Assess,			session, 2								
Respond,			hours total								
Empower											
(continued)			P-CARE, 2								
(**************************************			sessions, 2								
			hours total								
			Tiodio total								
			C-Care plus								
			P-CARE, 1								
			child session,								
			2 hours total;								
			2 parent								
			sessions, 2								
			hours total								

Abbreviations: ASQ-R=Adolescent Suicide Questionnaire—Revised; BDI-II=Beck Depression Inventory, version 2; BHS=Beck Hopelessness Scale; BSS=Beck Scale for Suicide Ideation; C-Care=Counselors Care, Assess, Respond, Empower; CAFAS=Child and Adolescent Functional Assessment Scale; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CES-D=Center for Epidemiological Studies-Depression; CG=control group; CGAS=Children's Global Assessment Scale; CI=confidence interval; DBT=dialectical behavioral therapy; G=group; GHQ=General Health Questionnaire, 12 questions; HSFC=Hopelessness Scale for Children; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; HSFC=Hopelessness Scale for Children; IG=intervention group; IG=intervention group; MADRS=Montgomery-Åsberg Depression Rating Scale; MBT=mentalization-based therapy; MFQ=mood & feelings questionnaire; N=number; NA=not applicable; NR=not reported; NS=not significant; OR=odds ratio; P-Care=Parents-Counselors Care, Assess, Respond, Empower; PQ-LES=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; RADS-2=Reynolds Adolescent Depression Scale, 2nd Edition: Short Form; RAP-P=Resourceful Adolescent Parent Program; RCADS MD=Revised Children's Anxiety and Depression Scale-Depression; SD=standard deviation; SDQ=Strengths and Difficulties Questionnaire; SE=standard error; SIQ=Suicidal Ideation Questionnaire; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; SMFQ=Short Mood and Feelings Questionnaire; SSI=Scale for Suicidal Ideation; vs.=versus.

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	ADIS CSR primary diagnosis	10	56	2.16 (SD: 2.59)	53	5.45 (SD: 1.90)	Partial eta squared=0.35	<0.001
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	ADIS CSR all diagnosis	10	56	5.21 (SD: 5.19)	53	10.75 (SD: 5.63)	Partial eta squared=0.22	<0.001
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	SCAS-youth	10	56	21.57 (SD: 14.42)	53	32.55 (SD: 15.64)	Partial eta squared=0.18	<0.001
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	SCAS-P mother	10	56	22.25 (SD: 12.59)	53	37.04 (SD: 16.95)	Partial eta squared=0.24	<0.001
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	SCAS-P father	10	56	23.56 (SD: 13.87)	53	32.63 (SD: 16.17)	Partial eta squared=0.19	<0.001
	Asbrand et al, 2020 ⁶⁷	11.3	Exposure- based group CBT, 12 weeks	SPAI-C	12	31	NR	36	NR	F(2,116.6)=5.87	0.004
	Asbrand et al, 2020 ⁶⁷	11.3	Exposure- based group CBT, 12 weeks	SASC-R child	12	31	NR	36	NR	F(2,115.6)=1.16	0.316
	Asbrand et al, 2020 ⁶⁷	11.3	Exposure- based group CBT, 12 weeks	SASC-R parent	12	31	NR	36	NR	F(2,114.4)=1.01	0.366

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT (continued)	Cornacchio et al, 2019 ⁷⁹	6.6	program that	ADIS CSR selective mutism	4	14	4.2 (SD: 0.9)	15	4.6 (SD: 0.7)	Effect size Cohen's d=-0.50	>0.05
	Cornacchio et al, 2019 ⁷⁹	6.6		ADIS CSR social anxiety	4	14	4.0 (SD: 0.8)	15	4.0 (SD: 0.8)	Effect size Cohen's d=-0.50	>0.05
	al, 2019 ⁷⁹	6.6	program that relies on the early child format of Parent Child Interaction Therapy, 5 days	SMQ-P home subscale			2.2 (SD: 0.4)		1.7 (SD: 0.7)	Cohen's d=0.36	>0.05
	Cornacchio et al, 2019 ⁷⁹	6.6		SMQ-P social subscale	4	14	1.2 (SD: 0.6)		0.7 (SD: 0.7)	Cohen's d=0.58	<0.05

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT (continued)	Holmes et al, 2014 ⁹⁹	9.6		ADIS-C/P CSR	10	17	3.59 (SD: 1.3)	19	6.21 (SD: 0.79)	Partial-eta squared=0.43	<0.001
	Holmes et al, 2014 ⁹⁹	9.6		SCAS-P GAD symptoms	10	20	NR	22	NR	Partial eta squared=0.09	0.048
	Holmes et al, 2014 ⁹⁹	9.6		SCAS-P GAD symptoms	10	17	6.17 (SD: 2.71)	19	6.84 (2.29)	NR	0.053
	Holmes et al, 2014 ⁹⁹	9.6	•	SCAS-P total symptoms	10	17	29.94 (SD: 12.70)	19	31.47 (SD: 8.79)	NR	P=NS
	Holmes et al, 2014 ⁹⁹	9.6		SCAS-C GAD symptoms	10	17	7.41 (SD: 4.65)	19	8.42 (SD: 4.56)	NR	P=NS

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT (continued)	Holmes et al, 2014 ⁹⁹	9.6	Group CBT program termed "No Worries!" that utilizes the A- B-C model, 10 weeks	SCAS-C total symptoms	10	17	34.88 (SD: 20.25)	19	40.84 (SD: 19.93)	NR	P=NS
	Lau et al, 2010 ¹¹⁰	8 years 7 months	Coping Cat CBT group- treatment program, 11 weeks	SCAS-C	13	24	10.5) (9.7 decrease from baseline)	21	38.8 (SD: 13.7) (1.8 increase from baseline)	Effect size partial eta squared=0.27	<0.001
	Lau et al, 2010 ¹¹⁰	8 years 7 months	Coping Cat CBT group- treatment program, 11 weeks	SCAS-P	13	24	28.8 (SD: 10.3) (decrease 4.2 from baseline);	21	36.5 (SD: 11.0) (increase 1.3 from baseline)	Effect size partial eta squared=0.11	<0.05
	Sanchez- Garcia et al, 2009 ¹³¹	11.91	Group CBT referred to as Intervencion en Adolescentes con Fobia Social, 12 weeks	SPAI-C	12	IG1: 28 IG2: 29	IG1: 15.45 (SD: 7.77); IG2: 12.75 (SD: 8.03);	25	30.80 (SD: 5.75)	IG1 vs. CG: effect size=2.23 IG2 vs. CG: effect size=2.51	IG1 vs. CG <0.001 IG2 vs. CG <0.001
	Sanchez- Garcia et al, 2009 ¹³¹	11.91		SPAI-C	24	IG1: 28 IG2: 29	IG1:11.91 (SD: 6.03) IG2: 13.21 (SD: 8.55)	25	27.64 (SD: 4.01)	IG1 vs. CG: effect size=3.04 IG2 vs. CG effect size=2.08	IG1 vs. CG <0.001 IG2 vs. CG <0.001
	Sanchez- Garcia et al, 2009 ¹³¹	11.91	Group CBT referred to as Intervencion en Adolescentes con Fobia Social, 12 weeks	SASC-R	12	IG1: 28 IG2: 29	IG1: 15.89 (SD: 6.81) IG2: 11.45 (SD: 6.48)	25	35.36 (SD: 5.33)	IG1 vs. CG: effect size=3.16 IG2 vs. CG effect size=3.94	IG1 vs. CG <0.001 IG2 vs. CG <0.001

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT (continued)	Sanchez- Garcia et al, 2009 ¹³¹	11.91	Group CBT referred to as Intervencion en Adolescentes con Fobia Social, 12 weeks		24	IG1: 28 IG2: 29	IG1:12.14 (SD: 6.86) IG2: 12.24 (SD: 7.34)	25	,	IG2 vs. CG effect size=2.90	<0.001 IG2 vs. CG <0.001
Individual CBT	Barrett et al, 1996 ⁷⁰	9.3	Individual CBT using using Coping Koala Workbook, 12 weeks		12	28	IG1: 9.0 (6.8) IG2: 6.6 (4.6)	23	11.6 (SD: 6.0)	NR	IG1 vs. CG: P=NS IG2 vs. CG: P=NS
	Barrett et al, 1996 ⁷⁰	9.3	Individual CBT using using Coping Koala Workbook, 12 weeks	FSSCR	12	28	IG1: 119.9 (26.0) IG2: 114.2 (20.2)	23	134.3 (SD: 32.6)	NR	IG1 vs. CG: P=NS IG2 vs. CG: P=NS
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks		12	148	3.97	68	4.15	NR	0.38
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	CGI-S	52	148	3.61	68	3.41	NR	0.34
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks		12	148	20.25	68	21.72	Cohen's d=0.29	0.05
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	SCARED-P	52	148	17.74	68	15.12	NR	0.44
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	SCARED-C	12	148	22.82	68	23.65	NR	0.87
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	SCARED-C	52	148	19.63	68	20.54	NR	0.65

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT (continued)	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks		10	20	1.9 (SD: 2.3)	20	5.7 (SD: 1.1)	Effect size partial eta squared=0.54	<0.001
	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks			20	15.2 (SD: 12.5)	20	46.3 (SD: 15.9)	Effect size partial eta squared=0.53	<0.001
	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks			20	18.9 (SD: 12.4)	20	14.9)	Effect size partial eta squared=0.37	<0.001
	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks	SCARED-R-C (GAD)	10	20	4.6 (SD: 5.2)	20	12.9 (SD: 4.2)	Effect size partial eta squared=0.47	<0.001
	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks	SCARED-R-P (GAD)	10	20	6.5 (SD: 4.3)	20	11.2 (SD: 4.7)	Effect size partial eta squared=0.24	<0.001
	Perrin et al, 2019 ¹²²	13.4;	Individual, GAD-specific CBT, 10 weeks	PSWQ-C	10	20	10.6 (SD: 12.2)	20	31.1 (SD: 7.2)	Effect size partial eta squared=0.4	<0.001
	Salzer et al, 2018 ⁴²	17.4	Individual CBT focused on reducing self- focused attentional and safety behaviors, 31 weeks	LSAS-CA change from baseline	Post- treatment	34	NR	39	NR	Effect size Cohen's d (95% CI); 0.61 (0.14 to 1.08)	0.0112
	Salzer et al, 2018 ⁴²	17.4	Individual CBT focused on reducing self- focused attentional and safety behaviors, 31 weeks	SPAI change from baseline	Post- treatment	34	NR	39	NR	Effect size Cohen's d (95% CI); 0.75 (0.27 to 1.22)	0.0021
	Villabo et al, 2018 ¹⁵⁰	10.5	Individual CBT using the Coping Cat manual, 12 weeks	MASC-child	12	IG1: 55; IG2: 55	IG1:48.61 (SE 1.48) IG2: 48.8 (SE: 1.65)	55	51.95 (SE: 1.60)	Hedges g (95% CI); IG1 vs CG:	IG1 vs CG: P=NS; IG2 vs. CG: P=NS

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT (continued)	Villabo et al, 2018 ¹⁵⁰	10.5	Individual CBT using the Coping Cat manual, 12 weeks	MASC-parent	12	IG1: 55 IG2: 55	IG1: 47.25 (SE: 2.58) IG2: 49.72 (SE: 2.46)	55	50.86 (SE: 2.45)	CI); IG1 vs. CG:	IG1 vs CG: P=NS; IG2 vs. CG: P=NS
Individual CBT, Sertraline, Individual CBT+Sertraline	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	PARS change from baseline	12	IG1: 139 IG2: 133 IG3: 140	IG1: 10.8 (SD: 5.9) IG2: 9.8 (SD: 6.2) IG3: 7.4 (SD: 6.0)	76	12.6 (SD: 6.3)	IG1 vs. CG: Effect size Hedge's g (95% CI): 0.31 (0.02 to 0.59); IG2 vs.	P=NS; IG3 vs. CG: P=NS
	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	CGI-S change from baseline	12	IG1: 139 IG2: 133 IG3: 140	IG1: 3.3 (SD: 1.3) IG2: 3.0 (SD: 1.3) IG3: 2.4 (SD: 1.3)	76	3.8 (SD: 1.4)	NR	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT, Sertraline, Individual CBT+Sertraline (continued)	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	MASC-C	12		IG1: 40.9 (SD: 10.4) IG2: 38.2 (SD: 10.7) IG3: 39.5 (10.8)	76	`	IG2 vs. CG: b=-4.68, t=-2.80	IG2 vs. CG: adjusted P=0.03; All other comparisons not statistically significant, P NR
	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	MASC-P	12		IG1: 42.1 (SD: 16.1) IG2: 37.9 (SD: 17.3) IG3: 33.4 (SD: 16.9)	76	49.1 (SD: 16.9)	IG3 vs. CG:	IG1 vs. CG; adjusted P<0.001; IG2 vs. CG; adjusted P<0.001; IG3 vs. CG: adjusted P<0.001

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT, Sertraline, Individual CBT+Sertraline (continued)	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon- Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	SCARED-C	12	IG1: 139 IG2: 133		76		NR	No statistically significant differences between arms, P NR;
	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	SCARED-P	12	IG1: 139 IG2: 133 IG3: 140	IG1: 16.9 (SD: 11.2) IG2: 11.0 (SD: 11.7) IG3: 9.6 (SD: 11.4)	76	19.5 (SD: 11.8)	IG1 vs. CG: NR IG2 vs. CG: b=-7.9, t=-4.7 IG3 vs. CG: b=-9.8, t=-5.9	IG1 vs. CG: adjusted P=0.26; IG2 vs. CG: adjusted P<0.001; IG3 vs. CG: adjusted P<0.001
	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	CSR change from baseline	12	IG1: 16 IG2: 16	IG1: 3.25 (SD: 0.39) IG2: 3.69 (SD: 1.66)		5.95 (SD: 1.15)	F=26.6	<0.001; IG1 vs. CG: P=sig, NR, favoring IG1; IG2 vs. CG: P=sig, NR, favoring IG2

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT, Sertraline, Individual CBT+Sertraline (continued)	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	SPAI-C change from baseline	12	IG1: 16 IG2: 16	IG1: 12.5 (SD: 8.9) IG2: 19.1 (SD: 12.0)	23	9.4)	F=5.0	<0.05; IG1 vs. CG: P=sig, NR, favoring IG1; IG2 vs. CG: P=sig, NR, favoring IG2
	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	MASC change from baseline			IG1: 35.8 (SD: 16.0) IG2: 43.2 (SD: 18.1)	23	15.3)	F=4.6	<0.05; IG1 vs. CG: P=sig, NR, favoring IG1; IG2 vs. CG: P=NS
	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	CDI change from baseline	12	IG1: 16 IG2: 16	IG1: 6.4 (SD: 6.1) IG2: 9.3 (SD: 9.7)	23	7.7)	F=1.2	P=NS
	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	SPAI-P change from baseline	12	IG1: 16 IG2: 16	IG1: 19.8 (SD: 10.7) IG2: 24.6 (SD: 12.5)	23	29.8 (SD: 8.7)	F=4.2;	<0.05; IG1 vs. CG: P=sig, NR, favoring IG1; IG2 vs. CG: P=NS

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT, Sertraline, Individual CBT+Sertraline (continued)	Ost et al, 2015 ²¹²	11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	FSSCR change from baseline	12	IG1: 16 IG2: 16	IG1: 109.1 (SD: 23.7) IG2: 117.3 (SD: 30.2)	23	119.3 (SD: 32.6)	F=0.8	>0.05; IG1 vs. CG: P=NS; IG2 vs. CG: P=NS
Internet CBT	Donovan et al, 2014 ⁸³	4.1	Online individual parent-focused CBT, 8 weeks	CSR	8	23	3.4 (SD: 2.4)	27	4.7 (SD: 2.0)	Partial eta squared=0.176 (mITT) 0.188 (ITT)	0.002 (mITT) 0.001 (ITT)
	Donovan et al, 2014 ⁸³	4.1	Online individual parent-focused CBT, 8 weeks	PAS	8	19	30.0 (SD: 14.7)	29	40.2 (SD: 17.0)	Partial eta- squared=0.131 0.066 (mITT)	0.011 (mITT) 0.66 (ITT)
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and	ADIS-DSM IV CSR (primary diagnosis) change from baseline	14	35	NR	35	NR	Cohen's d=0.65;	0.022
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety	anxiety		35	NR	35	NR	Cohen's d=0.83	0.002
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	SCAS-C change from baseline	14	35	NR	35	NR	Cohen's d=0.68	<0.001

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Group Difference	Between- Group P Value
Internet CBT (continued)	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	SCAS-M change from baseline	14	35	NR	35	NR	Cohen's d=1.12	<0.001
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	SCAS-F change from baseline	14	35	NR	35	NR	Cohen's d=0.46	0.011
	Waite et al, 2019 ¹⁵²	14.7	Internet CBT with accompanying parent sessions for half the group and no parent sessions for the other half, 10 weeks	CSR change from baseline	17	30	3.89 (SD: 2.58)	30	4.86 (SD: 2.19)	Effect size=0.05 (95% CI, 0.00 to 0.19)	NR
	Waite et al, 2019 ¹⁵²	14.7	Internet CBT with accompanying parent sessions for half the group and no parent sessions for the other half, 10 weeks	SCAS-C change from baseline	17	30	30.35 (SD: 19.17)	30	33.46 (SD: 15.01)	Effect size=0.05 (95% CI, 0.00 to 0.20)	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Internet CBT (continued)	Waite et al, 2019 ¹⁵²	14.7	Internet CBT with accompanying parent sessions for half the group and no parent sessions for the other half, 10 weeks	SCAS-P change from baseline	17	30	33.12 (SD: 21.70)	30	28.93 (SD: 15.79)	Effect size=0.06 (95% CI, 0.00 to 0.21)	NR
Parent-only CBT	Cobham et al, 2017 ⁷⁷	9.3	Parent-only group-based CBT sessions, 6 weeks	ADIS-CSR	6	33	3.7 (SD: 2.6)	29	5.4 (SD: 1.1)	NR	<0.001
	Cobham et al, 2017 ⁷⁷	9.3	Parent-only group-based CBT sessions, 6 weeks	SCAS-M	6	33	20.1 (SD: 4.9)	29	32.3 (SD: 11.9)	NR	<0.001
	Cobham et al, 2017 ⁷⁷	9.3	Parent-only group-based CBT sessions, 6 weeks	SCAS-F	6	33	21.4 (SD: 14.4)	29	30.6 (SD: 15.2)	NR	0.53
	Cobham et al, 2017 ⁷⁷	9.3	Parent-only group-based CBT sessions, 6 weeks	SCAS-C	6	33	34.4 (SD: 13.9)	29	42.1 (SD: 11.5)	NR	<0.01
Parent-only and parent-child CBT	Hirshfeld- Becker et al, 2010 ⁹⁸	5.4	Being Brave manualized CBT intervention with parent- only and parent-child sessions, 6 months	CGI-I SocAD score	24	19	2.42 (SD: 0.96)	20	3.40 (SD: 1.05)	Hedge's g=0.95 (95% CI, 0.29 to 1.62)	<0.01

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-only and parent-child CBT (continued)	Hirshfeld- Becker et al, 2010 ⁹⁸	5.4	manualized CBT intervention with parent- only and parent-child sessions, 6 months	CGI-I S SepAD score	24	12	1.67 (SD: 0.98)	13	2.46 (SD: 0.88)	Hedge's g=0.82 (95% CI, 0.01 to 1.64)	0.045
	Hirshfeld- Becker et al, 2010 ⁹⁸	5.4		CGI-I GAD score	24	12	2.17 (SD: 0.83)	12	2.58 (SD: 1.38)	NR	0.38
	Becker et al, 2010 ⁹⁸	5.4	manualized CBT intervention with parent- only and parent-child sessions, 6 months	CGI-I specific phobia score	24	15	1.87 (SD: 1.30)	15	2.87 (SD: 1.19)	Hedge's g=0.78 (95% CI, 0.04 to 1.52)	
	Hirshfeld- Becker et al, 2010 ⁹⁸	5.4	manualized	CGI-I agoraphobia score	24	9	2.22 (SD: 0.83)	11	2.55 (SD: 1.45)	NR	0.58

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-child CBT	Ishikawa et al, 2019 ¹⁰³	10.9	Japanese Anxiety Children/ Adolescents Cognitive Behavior; Therapy program, 8 weeks, with up to 3 subsequent booster sessions until 6 months after completion of therapy		8 or 16 (post- treatment)	25	28.28 (SE: 3.55)	24	35.95 (SE: 3.97)	NR	P=NS
	Ishikawa et al, 2019 ¹⁰³	10.9	Japanese Anxiety Children/	CSR on primary diagnosis	8 or 16 (post- treatment		3.08 (SE: 0.50)	24	6.0 (SE: 0.51)	NR	<0.001 favoring CBT

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	(SD/SE)	Placebo; N	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-child CBT (continued)	Ishikawa et al, 2019 ¹⁰³	10.9	Japanese Anxiety Children/ Adolescents Cognitive Behavior; Therapy program, 8 weeks, with up to 3 subsequent booster sessions until 6 months after completion of therapy	SCAS-P	8 or 16 (post- treatment	25	25.42 (SE: 2.57)	24	27.57 (SE: 2.62)	NR	<0.01 favoring CBT
Parent-guided CBT supported by telephone	Lyneham et al, 2006 ¹¹²	9.4	Parent-guided CBT supported by telephone using self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion, 12 weks	anxiety	12	IG1: 28 IG2: 21 IG3: 29	NR	22		IG1 vs. CG: Effect size cohen's d=2.19 IG2 vs. CG: Effect size cohen's d=1.57 IG3 vs. CG: Effect size cohen's d=0.80 Across all groups: Eta squared=0.49	IG1 vs. CG: <0.01; IG2 vs. CG: <0.01; IG3 vs. CG: <0.01; Across all groups: <0.01

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-guided CBT supported by telephone (continued)	Lyneham et al, 2006 ¹¹²	9.4	Parent-guided CBT supported by telephone using self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion, 12 weks		12	IG2: 21 IG3: 29	IG1: 39.50 (SD: 14.94) pretreat- ment 20.36 (SD: 16.04) 12 weeks IG2: 36.00 (SD: 14.57) pretreat- ment; 21.29 (SD: 14.28) 12 weeks IG3: 34.97 (SD: 15.50) pretreat- ment 22.97 (SD: 15.20) 12 weeks	22	39.23 (SD: 13.89) pretreat- ment 37.77 (SD: 15.26) 12 weeks	NR	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Group Difference	Between- Group P Value
Parent-guided CBT supported by telephone (continued)	Lyneham et al, 2006 ¹¹²	9.4	Parent-guided CBT supported by telephone using self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion, 12 weks		12		IG1: 32.46 (SD: 14.48) pretreat- ment 22.50 (SD: 13.48) 12 weeks IG2: 26.47 (SD: 9.91) pretreat- ment 18.76 (SD: 10.37) 12 weeks IG3: 29.80 (SD: 16.90) pretreat- ment 19.60 (SD: 13.45) 12 weeks	22	28.33 (SD: 17.68) pre- treatment 29.50 (SD: 18.39) 12 weeks	NR	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-guided CBT supported by telephone (continued)	Lyneham et al,	9.4	Parent-guided CBT supported by telephone using self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion, 12 weks	SCAS-C	12	IG1: 28 IG2: 21 IG3: 29	IG1: 43.54 (SD: 16.65) pretreat- ment 23.79 (SD: 14.84) 12 weeks IG2: 35.90 (SD: 12.13) pretreat- ment 24.86 (SD: 12.94) 12 weeks IG3: 35.17 (SD: 20.66) pretreat- ment 25.79 (SD: 19.51) 12 weeks			NR	NR
	Lyneham et al, 2006 ¹¹²	9.4	Parent-guided CBT supported by telephone using self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion, 12 weks	RCMAS-C	12			22	15.59 (SD: 7.57) pretreat- ment 15.73 (SD: 7.30) 12 weeks	NR	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo;	Placebo; Score (SD/SE)	Between- Group Difference	Between- Group P Value
Parent-delivered CBT	Rudy et al, 2017 ¹²⁹	5.36	therapy first led by a therapist and then led by a parent, 5 weeks		5	12	2.72 (SD: 1.56)	10	1.81)	Effect size d=2.39	0.009
	Rudy et al, 2017 ¹²⁹	5.36	therapy first led by a therapist and then led by a parent, 5 weeks		5	12	2.00 (SD: 0.89)		3.33 (SD: 0.71)	Effect size d=2.75	<0.001
	Rudy et al, 2017 ¹²⁹	5.36	therapy first led by a therapist and then led by a parent, 5 weeks		5	12	9.72 (SD: 4.76)	10	15.78 (SD: 3.35)	Effect size d=3.18	0.046
	Thirlwall et al, 2013 ¹⁴⁵	NR, partici- pants ages 7 to 12 years	delivered CBT with a self-help book, 8 weeks		12	IG1: 38 IG2: 42	IG1: 24.16 (SD: 12.93) IG2: 20.45 (SD: 11.52)	46	24.15 (SD: 11.36)	NR	IG1 vs. CG: P=NS; IG2 vs. CG: P=NS
	Thirlwall et al, 2013 ¹⁴⁵	NR, partici- pants ages 7 to 12 years	delivered CBT with a self-help book, 8 weeks		12	IG1: 40 IG2: 47	(SD: 12.6) IG2: 28.47 (SD: 20.0)	57	29.40 (SD: 16.28)	NR	IG1 vs. CG: P=NS; IG2 vs. CG: P=NS
Family-based CBT	Shortt et al, 2001 ¹³⁴	7.9	Family Based Cognitive Behavioral therapy sessions termed "FRIENDS," adapted from Coping Koala Workbook, 10 weeks	RCMAS	10	53	8.6 (SD: 0.97)	12	9.8 (SD: 2.0)	Eta squared=0.10	<0.05

		Mean			Time	_	Treatment		Placebo;		Between-
Treatment		Age	Intervention	Outcome	Point	Treatment	Score	Placebo;	Score	Group	Group P
(Condition)	Author, Year	(Years)	and Duration	Measure	(Weeks)	N	(SD/SE)	N	(SD/SE)	Difference	Value
Family-based	Shortt et al,	7.9	Family Based	DISCAP CSR	10	48	1.06 (SD:	16	4.13 (SD:	Eta	<0.001
CBT (continued)	2001134		Cognitive				0.24)		0.41)	squared=0.46	
			Behavioral						-		
			therapy								
			sessions								
			termed								
			"FRIENDS,"								
			adapted from								
			Coping Koala								
			Workbook, 10								
			weeks								

Abbreviations: ADIS-C/P=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children/Parents; ADIS CSR=Anxiety Disorders Interview Schedule clinician severity ratings; ADIS-DSM=Anxiety and Related Disorders Interview Schedule--Diagnostic and Statistical Manual; CBT=cognitive behavioral therapy; CDI=Children's Depression Inventory; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; CSR=Clinician Severity Rating; DISCAP=Diagnostic Interview Schedule for Children, Adolescents, and Parents; DSM IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; FSSCR=Fear Survey Schedule for Children-Revised; GAD=general anxiety disorder; IG=intervention group; ITT=intention to treat; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; MASC-child=Multidimensional Anxiety Scale for Children; MASC-parent=Multidimensional Anxiety Scale for Parents; mITT=modified intent to treat; N=number; NR=not reported; NS=not significant; PARS=Pediatric Anxiety Rating Scale; PAS=Preschool Anxiety Scale; PSWQ-C=Penn State Worry Questionnaire for Children; RCMAS=Revised Children's Manifest Anxiety Scale; RCMAS-C=Revised Children's Manifest Anxiety Scale; SASC-R=Social Anxiety Scale for Children-Revised; SCARED-C=Screen for Anxiety Related Emotional Disorders for Children's Anxiety Scale Revised-Child-rated; SCAS-C=Spence Children's Anxiety Scale Revised-Parent-rated; SCAS-R=Spence Children's Anxiety Scale Revised-Parent-rated; SCAS-R=Spence Children's Anxiety Scale Revised-Parent-rated; SCAS-R=Spence Children's SPAI-C=Social Phobia and Anxiety Inventory for Children for Parents; vs.=versus.

Appendix F Table 4. Anxiety Pharmacotherapy Interventions vs. Placebo: Anxiety Symptoms

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
	Strawn et al, 2015 ¹⁴²	12.4	Flexibly dosed duloxetine (30–120 mg/d)	PARS (severity for GAD)	10	135	-9.7 (SE: 0.5)	137 [*]	-7.1 (SE: 0.5)		≤0.001 [†]
				Change in PARS severity total score	10	135	-9.2 (SE: 0.5)	137 [*]	-6.4 (SE: 0.5)		≤0.001 [†]
				Change in CGI-S	10	135	-1.9 (SE: 0.1)	137 [*]	-1.4 (0.1)	NR	≤0.001†
	Strawn et al, 2020 ¹⁴³	14.8	Forced titration to 15 mg/d, then flexible titration to 20 mg/d	Change in PARS	8	26	-8.65 (SD: 1.31)	25	-3.52 (SD: 1.06)	NR	0.005†
				CGI-S	8	26	2.8 (SD: 0.3)	25	3.6 (SD: 0.2)	NR	<0.001†
	Birmaher et al, 2003 ⁷³	11.8	10 mg/d, after first week, up to 20 mg/d	SCARED-C	12	37	11.7 (SD: 12.4)	37	12.10 (SD: 7.3)	NR	0.03 [†]
				SCARED-P	12	37	16.3 (SD: 12.7)	37	22 (SD: 12.3)	NR	0.04 [†]
				PARS	12	37	7.1 (SD: 5.9)	37	9.3 (SD: 4.8)	NR	0.007† (0.08 for post-test differences)
(GAD, SepAD, or SocAD)	Pine et al, 2001 ¹²⁴ Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵		50 mg/d, then increase 50 mg/w to max. 300 mg/d in adolescents (13-17 years) and 250 mg/d in children ≤12 years of age		8	63	9.0 (SD: 7.0)	65	15.9 (SD: 5.3)	NR	<0.001†
	Rynn et al, 2001 ¹³⁰	11.7	25 mg/d for the first week and 50 mg/d for weeks 2 to 9	HAM-A	9	11	7.8 (SD: 5.7)		21.0 (SD: 7.8)	NR	<0.001†
				CGI-S	9	11	2.4 (SD: 0.8)		3.9 (SD: 0.3)		<0.001†
				CGI-I	9	11	2.1 (SD: 1.1)	11	3.5 (SD: 0.7)	NR	0.001

Appendix F Table 4. Anxiety Pharmacotherapy Interventions vs. Placebo: Anxiety Symptoms

Treatment (Condition)	Author, Year	Mean Age (Years)	Dose	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Sertraline (GAD) (continued)	,			ADIS CSR-C	9	11	2.7 (SD: 2.0)	11	4.6 (SD: 2.0)	NR	0.11‡
				ADIS CSR-P	9	11	2.6 (SD: 1.7)	11	4.9 (SD: 2.0)	NR	<0.007‡
				RCMAS	9	11	8.9 (SD: 7.0)		14.6 (SD: 8.2)	NR	<0.02‡
				MASC	9	11	35.7 (SD: 17.2)	11	56.4 (SD: 16.3)	NR	<0.03 [‡]
SepAD, or SocAD)	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	25mg/d, up to 200 mg/d by 8th week	PARS	12	133	9.8 (SD: 6.2)	76	12.6 (SD: 6.3)	Hedge's g (95% CI): 0.45 (0.17 to 0.74)	S
				CGI-S	12	133	3.0 (SD: 1.3)	76	3.8 (1.4)	NR	CIs of individual treatments do not overlap
				MASC-C	12	133	38.2 (SD: 10.7)	76	42.9 (11.8)	b=-4.68, t=-2.80	0.03
				MASC-P	12	133	37.9 (SD: 17.3)	76	49.1 (16.9)	b=-11.1, t=-4.4	<0.001
				SCARED-C	12	133	9.3 (SD: 11.9)	76	13.8 (12.1)	NR	p=NS, p=NR
				SCARED-P	12	133	11.0 (SD: 11.7)	76	19.5 (11.8)	NR	<0.001

^{*} N randomized=137, N analyzed=133. Conversion of standard error to standard deviation based on N analyzed.

 $^{^\}dagger \mbox{Difference}$ in change from baseline to follow up.

[‡] Difference at followup.

Appendix F Table 4. Anxiety Pharmacotherapy Interventions vs. Placebo: Anxiety Symptoms

Abbreviations: ADIS=Anxiety Disorders Interview Schedule; ADIS-CSR=Anxiety Disorders Interview Schedule Clinician Severity Rating CGI=Clinical Global Impressions; CI=confidence interval; CSR-C=clinical severity score-child-rated; CSR-P= clinical severity score-parent-rated; GAD=generalized anxiety disorder; HAM-A=Hamilton Anxiety Rating Scale; MASC=Multidimensional Anxiety Scale for Children; N=number; NR=not reported; NS=not statistically significant; PARS=Pediatric Anxiety Rating Scale; RCMAS=Revised Children's Manifest Anxiety Scale; SCARED-C=Screen for Anxiety Related Emotional Disorders Child version; SCARED-P=Screen for Anxiety Related Emotional Disorders - Parent version; SD=standard deviation; SE=standard error; SepAD=separation anxiety disorder; SocAD=social anxiety disorder; vs.=versus.

Treatment (Condition)	Author, Year, Trial Number	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	N	N (%)	Placebo N	N (%)	Effect measure (95% CI), p value
Group child+parent in- person CBT	Cornacchio et al, 2019 ⁷⁹	6.6	5 days	CGI-I≤2	4	14	7 (50)	15	0 (0)	(-0.58), P≤0.01
Individual child- focused in- person CBT	Ginsburg et al, 2020 ⁹²	10.9	12 weeks	CGI-I≤2	12	148	NR (42.1)	68	NR (36.7)	P=0.34
Individual child- focused in- person CBT	Salzer et al, 2018 ⁴² ISRCTN 22752528	17.4	31 weeks	LSAS-CA ≥31% reduction in total score	Post- treatment	34	NR (66)	39	NR (20)	(2.17 to 28.86), P=0.006
Individual child- focused in- person CBT	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	12 weeks	CGI-I ≤2	12		83 (59.7)	76		(2.5 to 9.0), P<0.001
Individual child- focused internet CBT	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	Clinically reliable change in SCAS-C	14	32	22 (69)	31	8 (26)	P=0.001

Treatment (Condition)	Author, Year, Trial Number	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect measure (95% CI), p value
	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	Clinically reliable change in SCAS-M	14	35	24 (69)	32	7 (22)	P<0.001
	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	Clinically reliable change in SCAS-F	14	25	9 (35)	27	5 (19)	P=0.156
Individual child+parent in- person CBT	Hirshfeld- Becker et al, 2010 ⁹⁸	5.4	6 months	CGI-I ≤2	6 months	34	20 (59)	30	9 (30)	P=0.016
Individual parent- led in-person CBT	Rudy et al, 2017 ¹²⁹ NCT02051192	5.36	5 weeks	CGI-I ≤2	5	12	10 (83.3)	10	0 (0.0)	P<0.001
with and without parent sessions	Waite et al, 2019 ¹⁵² ISRCTN79652741		10 weeks	CGI ≤2	17	30	12 (40.0)	30	9 (30.0)	(0.53-4.53)

Abbreviations: CBT=cognitive behavioral therapy; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; NR=not reported; SCAS-C=Spence Children's Anxiety Scale-Child-rated; SCAS-F=Spence Children's Anxiety Scale -Father; SCAS-M=Spence Children's Anxiety Scale -Mother; vs.=versus.

Treatment					Time Point	Treatment		Placebo		Effect Measure
(Condition)	Author, Year	Mean Age	Duration	Outcome Measure	(Weeks)	N	N (%)	N	N (%)	(95% CI), p value
Individual child- focused in- person CBT	Salzer et al, 2018 ⁴² ISRCTN 22752528	17.4	31 weeks	LSAS-CA ≤30	Post- treatment		NR (47)		NR (6)	(1.85 to 114.95), P=0.0009
Individual child- focused in- person CBT	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al,	10.7	12 weeks	CGI-S ≤2	12	139	50 (35.9)	76	21 (27.1)	(0 to 3.53), P=0.49
	2011 ²¹¹ Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon- Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	12 weeks	CGI-I=1	12	139	28 (20.4)	76	11 (15.0)	(0 to 4.78), P=0.61
Individual child+parent in- person CBT	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	SCAS-C; clinically significant change	2 or 4 months	25	14 (56.0)	24	9 (37.5)	P=0.20
F 5. 55.11	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	SCAS-P; clinically significant change	2 or 4 months	25	8 (32.0)	24	5 (20.83)	P=0.38

Treatment (Condition)	Author, Year	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p value
Individual child+parent in- person CBT (continued)	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	DSRS; clinically significant change	2 or 4 months	25	9 (36.0)	24	5 (20.83)	P=0.24
	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	CDI; clinically significant change	2 or 4 months	25	10 (40.0)	24	4 (16.67)	P=0.07
Individual child- focused internet CBT	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	SCAS-C; Clinically significant change	14	32	14 (44)	31	2 (6)	P=0.001
	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	SCAS-M; Clinically significant change	14	35	9 (26)	32	2 (6)	P=0.032
	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	SCAS-F; Clinically significant change	14	25	1 (4)	27	2 (7)	P=1.00
IG1: Individual child+parent telephone CBT IG2: Individual child+parent email CBT IG3: Individual child+parent client-initiated CBT	Lyneham et al, 2006 ¹¹² NR	9.4	12 weeks	SCAS-C normal range	12	IG1: 28 IG2: 21 IG3: 29	IG1: NR (62) IG2: NR (57) IG3: NR (50)	22	NR (23)	Any IG vs. CG: P<0.05
Individual parent-led in- person CBT	Rudy et al, 2017 ¹²⁹ NCT02051192	5.36	5 weeks	ADIS-CSR <4	5	12	8 (66.7)	10	1 (10.0)	P=0.011
Group child+parent in- person CBT	Arendt et al, 2016 ⁶⁵	11.8	10 weeks	Clinically significant change in SCAS-C	10	56	24 (42.9)	53	6 (11.3)	P≤0.001
	Arendt et al, 2016 ⁶⁵	11.8	10 weeks	Clinically significant change in SCAS-M	10	56	29 (51.8)	53	6 (11.3)	P≤0.001
	Arendt et al, 2016 ⁶⁵	11.8	10 weeks	Clinically significant change in SCAS-F	10	56	23 (41.8)	53	5 (9.8)	P≤0.001

Abbreviations: ADIS=Anxiety Disorders Interview Schedule for DSM-IV for Children; ADIS-CSR=Anxiety Disorders Interview Schedule for DSM-IV for Children Clinician Severity Rating; CBT=cognitive behavioral therapy; CDI=Children's Depression Inventory; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; DSRS=Depression Self-Rating Scale; IG=intervention group; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; N=number; NR=not reported; SCAS-C=Spence Children's Anxiety Scale-Child-rated; SCAS-F=Spence Children's Anxiety Scale-Child-rated-Female; SCAS-M=Spence Children's Anxiety Scale-Child-rated-Male; SCAS-P=Spence Children's Anxiety Scale-Parent-rated; vs.=versus.

Treatment (Condition)	Author, Year	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p value
Group child- focused in- person CBT	Holmes et al, 2014 ⁹⁹ ACTRN12612000061831	9.6	10 weeks	ADIS-C/P; absence of GAD diagnosis	10	17	NR (52.9)	19	NR (0)	P<0.001
	Holmes et al, 2014 ⁹⁹ ACTRN12612000061831	9.6	10 weeks	ADIS-C/P; absence of any anxiety diagnosis	10	17	NR (17.6)	19	NR (0)	P=0.056
Group child+parent in- person CBT	Arendt et al, 2016 ⁶⁵	11.8	10 weeks	ADIS-C/P; free of primary diagnosis	10	56	37 (66.1)	53	4 (7.5)	P<0.001
	Arendt et al, 2016 ⁶⁵	11.8	10 weeks	ADIS-C/P; free of all anxiety diagnoses	10	56	27 (48.2)	53	3 (5.7)	P<0.001
Group child+parent in- person CBT	Cornacchio et al, 2019 ⁷⁹	6.6	5 days	ADIS/C-P; Loss of selective mutism diagnosis	4	14	1 (7.1)	15	0 (0)	(0.19), P=1.00
Group child+parent in- person CBT	Lau et al, 2010 ¹¹⁰ NR	8 years 7 months	11 weeks	K-SADS; presence of anxiety diagnosis or symptoms	13	24	16 (67)	21	21 (100)	P<0.01
	Lau et al, 2010 ¹¹⁰ NR	8 years 7 months	11 weeks	K-SADS; absence of anxiety diagnosis or subclinical symptoms	13	24	8 (33)	21	0 (0)	NR
Group child+parent in- person CBT	Shortt et al, 2001 ¹³⁴	7.9	10 weeks	DISCAP; anxiety free diagnosis	10	48	33 (69)	16	1 (6)	P<0.001
Individual child- focused in- person CBT	Barrett et al, 1996 ⁷⁰	9.4	12 weeks	ADIS; no longer meeting criteria for current anxiety disorder	12	IG1/2: 53	37 (69.8)	23	6 (26.0)	P<0.05
Individual child- focused in- person CBT	Ginsburg et al, 2020 ⁹²	10.9	12 weeks	ADIS; no anxiety disorder	12	148	NR (34.9)	68	NR (35.0)	P=0.67

Treatment (Condition)	Author, Year	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p value
Individual child- focused in- person CBT (continued)	Ginsburg et al, 202092	10.9	12 weeks	ADIS; loss of primary anxiety disorder	12	148	NR (40.5)	68	NR (43.4)	P=0.61
Individual child- focused in- person CBT	Walkup et al, 2008 ¹⁵³ ; Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	12 weeks	ADIS-C/P; loss of anxiety diagnosis	12	139	64 (46.2)	76	18 (23.7)	(1.03 to 4.79), P=0.05
Individual child- focused internet CBT	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	ADIS; free of primary anxiety diagonsis	14	35	14 (40)	32	5 (16)	P=0.027
	Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	15	14 weeks	ADIS; free of any anxiety diagnosis	14	35	10 (29)	32	1 (3)	P=0.005
	Perrin et al, 2019 ¹²² ISRCTN50951795	13.4	10 weeks	ADIS; presence of GAD	10	20	4 (20)	20	20 (100)	P<0.001
	Perrin et al, 2019 ¹²² ISRCTN50951795	13.4	10 weeks	ADIS; presence of comorbid disorder	10	20	1 (5)	20	11 (55)	P<0.001
	Perrin et al, 2019 ¹²² ISRCTN50951795	13.4	10 weeks	ADIS; recovery from all disorders	10	20	16 (80)	20	0 (0)	P<0.000
Individual child + parent in-person CBT	Hirshfeld-Becker et al, 2010 ⁹⁸	5.4	6 months	SCID; absence of anxiety diagnosis	6 months	34	17 (50)	30	5 (17)	P<0.01
	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	ADIS; free of principal diagnosis	2 or 4 months	26	13 (50.0)	25	3 (12.0)	P<0.01
	Ishikawa et al, 2019 ¹⁰³	10.9	8 weeks	ADIS; free of any diagnosis	2 or 4 months	26	4 (15.38)	25	1 (4.0)	NS
Individual child+parent internet CBT	Waite et al, 2019 ¹⁵² ISRCTN79652741	14.7	10 weeks	ADIS-C/P; remission of primary anxiety diagnosis	17 weeks	30	12 (40.0)	30	7 (23.3)	(0.72 to 6.70)

Treatment (Condition)	Author, Year	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p value
Individual child+parent internet CBT (continued)	Waite et al, 2019 ¹⁵² ISRCTN79652741	14.7	10 weeks	ADIS-C/P; remission of all anxiety diagnoses	17 weeks	30	8 (26.7)	30	4 (13.3)	(0.63 to 8.92)
Parent-guided CBT supported by telephone	Lyneham et al, 2006 ¹¹² NR	9.4	12 weeks	ADIS; loss of prinicpal anxiety disorder	12	IG1: 28 IG2: 21 IG3: 29	NR	22	NR	Any IG vs. CG, P<0.01
	Lyneham et al, 2006 ¹¹² NR	9.4	12 weeks	ADIS; loss of any anxiety disorder	12	IG1: 28 IG2: 21 IG3: 29	NR	22	NR	Any IG vs. CG, P<0.01
Individual and group CBT, parent training	Ost et al, 2015 ¹²⁰	11.6	12 weeks	ADIS; no longer fufilling criteria for social phobia	12 months	IG1: 16 IG2: 16	IG1: 9 (56) IG2: 10 (62)	23	2 (9)	IG1 vs. CG: P≤0.001 IG2 vs. CG: P≤0.001
Individual CBT	Villabo et al, 2018 ¹⁵⁰ NR	10.5	12 weeks	ADIS; loss of primary anxiety diagnosis	12	IG1: 44 IG2: 52	IG1: NR (52) IG2: NR (65)	51	NR (14)	IG1 vs CG: (21 to 56), P<0.001 IG2 vs CG: (35 to 68), P<0.001
	Villabo et al, 2018 ¹⁵⁰ NR	10.5	12 weeks	ADIS; loss of all anxiety disorders	12	IG1: 44 IG2: 52	IG1: NR (38) IG2: NR (56)	51	NR (6)	IG1 vs CG: (16 to 47), P<0.001 IG2 vs CG: (34 to 65), P<0.001
Parent-delivered CBT full CBT	Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	NR; partici- pants ages 7 to 12 years	8 weeks	ADIS; loss of primary diagnosis	12	46	IG1: 18 (39) IG2: 25 (50)	63	16 (25)	IG1 vs. CG: (0.89 to 2.74), P=0.119 IG2 vs. CG: (1.14 to 2.99), P=0.013
	Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593		8 weeks	ADIS; loss of any diagnosis	12	46	IG1: 7 (15) IG2: 17 (34)	63	7 (11)	IG1 vs CG: (0.56 to 3.88), P=0.433 IG2 vs CG: (1.40 to 7.01), P=0.006
Group parent- only in-person CBT	Cobham et al, 2017 ⁷⁷ ACTRN12615000514505	9.3	6 weeks	ADIS; absence of primary diagnosis	6	31	20 (64.5)	29	5 (16.2)	(0.259 to 0.709), P<0.001
	Cobham et al, 2017 ⁷⁷ ACTRN12615000514505	9.3	6 weeks	ADIS; absence of any diagnosis	6	31	12 (38.7)	29	1 (3.4)	(0.47 to 0.82), P<0.001

Treatment (Condition)	Author, Year	Mean Age	Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p value
	Donovan et al, 2014 ⁸³ ACTRN12612000139875	4.1	8 weeks	ADIS; absence of primary diagnosis	8	23	9 (39)	27	7 (26)	P=0.318
	Donovan et al, 2014 ⁸³ ACTRN12612000139875	4.1		ADIS; absencse of any diagnosis	8	23	8 (35)	27	7 (26)	P=0.496

Abbreviations: ADIS=Anxiety Disorders Interview Schedule for DSM-IV for Children; ADIS-C/P=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children; ADIS-C/P=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children, Children, Parents; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; DISCAP=Diagnostic Interview Schedule for Children, Adolescents, and Parents; GAD=general anxiety disorder; IG=intervention group; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children; lifetime version; N=number; NR=not reported; NS=not significant; SCID=structured clinical interview; vs.=versus.

Appendix F Table 8. Anxiety Pharmacotherapy vs. Placebo for Anxiety in Children: Response

Treatment (Condition)	Author, Year	Mean Age	Dose (md/day)	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Escitalopram (GAD)	Strawn et al, 2020 ¹⁴³	14.8	Forced titration to 15 mg/d, then flexible titration to 20 mg/d, 8 weeks	CGI-I score ≤2	8	26	16 (62)	25	6 (24)	NR P=0.0039
Fluoxetine (GAD, SepAD, or social phobia)	Birmaher et al, 2003 ⁷³	11.8	Fluoxetine 10 mg/day, after first week increasing to 20 mg/day if tolerated	CGI-I score ≤2	12	36	22 (61)	37	13 (35)	Effect size=0.26 P=0.03
Fluoxetine (selective mutism)	Black et al, 1994 ⁷⁴	8.5	Fluoxetine 0.2 mg/kg for 1 week, then 0.4 mg/kg for 1 week, then 0.6 mg/kg for 10 weeks	CGI-I score ≤2	12	6	3 (50)	9	4 (44.4)	NR P=NS
Sertraline (GAD)	Rynn, 2001 ¹³⁰	11.7	25 mg for the first week and 50 mg for weeks 2 to 9, 9 weeks	CGI-I score ≤2	9	11	10 (91)	11	1 (9)	NR P<0.0001
Sertraline (GAD, SepAD, or SocAD)	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sanchez, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹ NCT00052078	10.7	25 mg/day, up to 200 mg/day by 8th week, for 12 weeks	CGI-I score ≤2	12	133	73 (54.9)	76	18 (23.7)	OR: 3.9 (3.0 to 5.9), P<0.001

Abbreviations: CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; GAD=general anxiety disorder; N=number; NR=not reported; NS=not significant; OR=odds ratio; SepAD=separation anxiety disorder; SocAD=social anxiety disorder; vs.=versus.

Appendix F Table 9. Anxiety Pharmacotherapy Interventions vs. Placebo: Remission

Treatment (Condition)	Author, Year	Mean Age	Dose (md/day)	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Duloxetine (GAD)	Strawn et al, 2015 ¹⁴²	12.4	Flexibly dosed duloxetine (30–120 mg/d)	≤2	10	135	(54)	133	(35)	NR P≤0.02
	Strawn et al, 2015 ¹⁴²	12.4	Flexibly dosed duloxetine (30–120 mg/d)	CGI-I score=1	10	135	(50)	133	(34)	NR P≤0.05
Sertraline (GAD)	Rynn et al, 2001 ¹³⁰	11.7	25 mg for the first week and 50 mg for weeks 2 to 9, 9 weeks	CGI-I score=1	9	11	2 (18)	11	0 (0)	NR P=0.28
Sertraline (GAD, SepAD, or SocAD)	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹ NCT00052078	10.7	25 mg/day, up to 200 mg/day by 8th week, for 12 weeks	CGI-S score ≤2	12	133	62 (46.3)	76	21 (27.1)	OR: 2.55 (0 to 5.48), P=0.29
	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹ NCT00052078	10.7	25 mg/day, up to 200 mg/day by 8th week, for 12 weeks	CGI-I score=1		133	,	76		OR: 3.56 (0 to 9.53), P=0.39
Sertraline (GAD, SepAD, or SocAD) (continued)	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Caporino et al, 2017 ²¹⁶ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹ NCT00052078	10.7	25 mg/day, up to 200 mg/day by 8th week, for 12 weeks	Loss of anxiety diagnosis	12	133	61 (45.9)	76	18 (23.7)	OR: 2.84 (1.01 to 4.67), P=0.05

Appendix F Table 9. Anxiety Pharmacotherapy Interventions vs. Placebo: Remission

Abbreviations: CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; GAD=general anxiety disorder; N=number; NR=not reported; OR=odds ratio; SepAD=separation anxiety disorder; SocAD=social anxiety disorder; vs.=versus.

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Group CBT	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	youth	10	56	6.46)	53	10.94 (SD: 7.20)	Partial eta squared=0.06	0.008
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	mother	10	56	7.28)	53	,	Partial eta squared=0.14	<0.001
	Arendt et al, 2016 ⁶⁵	11.8	Manualized group CBT program (Cool Kids), 10 weeks	father	10	56	10.96 (SD: 7.72)			Partial eta squared=0.11 F=12	<0.001
	Cornacchio et al, 2019 ⁷⁹	6.6	Group CBT program that relies on the early child format of Parent Child Interaction Therapy, 5 days	CGAS	4	14	53.6 (SD: 4.6)	15	52.5 (SD: 4.9)	Effect size Cohen's d=0.73	<0.1
	Holmes et al, 2014 ⁹⁹	9.6	Group CBT program termed "No Worries!" that utilizes the A-B-C model, 10 weeks	CGAS	10	17	63.82 (SD: 11.03)	19	51.05 (SD: 7.66)	Partial eta squared=0.15	0.02
	Holmes et al, 2014 ⁹⁹	9.6	Group CBT program termed "No Worries!" that utilizes the A-B-C model, 10 weeks	Pediatric QOL Inventory- C	10	17	76.09 (SD: 15.17)	19	66.88 (SD: 12.03)	NR	NS
	Holmes et al, 2014 ⁹⁹	9.6	Group CBT program termed "No Worries!" that utilizes the A-B-C model, 10 weeks	Pediatric QOL Inventory- P	10	17	79.17 (SD: 14.16)	19	75.34 (SD: 11.74)	NR	NS
Individual CBT	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	CGAS	12	148	55.98	68	54.22	NR	0.42
	Ginsburg et al, 2020 ⁹²	10.9	Individual CBT consisting of 7 core modules, 12 weeks	CGAS	52	148	58.92	68	59.22	NR	0.63
	Perrin et al, 2019 ¹²²	13.4	Individual, GAD- specific CBT, 10 weeks		10	20	8.9)	20	6.7)	Effect size partial eta squared=0.70	<0.001
	Perrin et al, 2019 ¹²²	13.4	Individual, GAD- specific CBT, 10 weeks	PQ-LES- Q	10	20	60.8 (SD: 10.7)	20	48.7 (SD: 9.4)	Effect size partial eta squared=0.23	<0.01

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT (continued)	Villabo et al, 2018 ¹⁵⁰	10.5	Individual CBT using the Coping Cat manual, 12 weeks	CGAS	12	IG1: 44 IG2: 52	IG1: 62.52 (SE: 1.17) IG2: 62.81 (SE: 1.10)	51	,	Effect size Hedge's g (95% CI) IG1 vs CG: 1.01 (0.68 to 1.35) IG2 vs CG: 1.04 (0.72 to 1.37)	IG1 vs CG <0.001 IG2 vs CG <0.001
Individual CBT, Sertraline, Individual CBT + Sertraline	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	CGAS		IG1: 139 IG2: 133 IG3: 140	IG1: 63.8 (SD: 10.2) IG2: 65.0 (SD: 10.7) IG3: 68.6 (SD: 10.4)	76	10.9)`	All active treatments noted to be superior to placebo	NR
	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	CAIS-C		IG1: 139 IG2: 133 IG3: 140	IG1: 9.1 (SD: 10.7) IG2: 7.7 (SD: 11.3) IG3: 8.1 (SD: 11.0)	76	11.5)	No statistically significant differences between arms	NR

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual CBT + Sertraline (continued)	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks	CAIS-P		IG1: 139 IG2: 133 IG3: 140	IG1: 13.5 (SD: 10.0) IG2: 9.1 (SD: 10.5) IG3: 7.4 (SD: 10.2)	76	15.2 (SD: 10.7)	IG2 vs. CG: b=-6.1, t=-4.0 IG3 vs. CG: b=-7.7, t=-5.2	IG1 vs. CG: adjusted P=0.27 IG2 vs. CG: adjusted P<0.001 IG3 vs. CG: adjusted P<0.001
	Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ; Compton et al, 2014 ²⁰⁷ ; Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ; Gordon-Hollingsworth et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹	10.7	Individual CBT using Coping Cat program adapted for child's age and length of the study, 12 weeks			IG1: 139 IG2: 133 IG3: 140	NR	76	NR	Active treatments resulted in significantly greater reductions in sleep problems than placebo related to separation, as reported by parents (F=6.52, p=0.01, η²=0.01) but not by children No significant treatment type x time interactions for parent- or child-rated dysregulated Sleep	Significantly greater reductions in sleep problems than placebo related to separation, P=0.01

Treatment (Condition)	Author, Year	Mean Age (Years)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Individual and group CBT, parent training		11.6	Individual weekly sessions and social skills group weekly sessions for the child and parent training about SocAD, 12 weeks	Change in QOLI-C from baseline	12	IG1: 16 IG2: 16	(SD: 1.84) IG2: 3.46 (SD: 1.63)	23	1.40)	F=4.1	<0.05 IG1 vs. CG=NS IG2 vs. CG=NS
Internet CBT	Donovan et al, 2014 ⁸³	4.1	Online individual parent-focused CBT, 8 weeks	CGAS	8	23	66.9 (SD: 10.6)	27	61.9 (SD: 10.0)	Partial eta squared=0.115	0.016
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	WHO-5 change from baseline	14	35	NR	35	NR	Effect size Cohen's d=0.04	0.945
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	CALIS-C change from baseline	14	35	NR	35	NR	Effect size Cohen's d=0.21	0.254
	Stjerneklar et al, 2019 ¹⁴¹	15	Internet CBT based on Cool Kids and Chilled anxiety management program, 14 weeks	CALIS-M change from baseline	14	35	NR	35	NR	Effect size Cohen's d=0.93	<0.001
	Stjerneklar et al, 2019 ¹⁴¹	15		CALIS-F change from baseline	14	35	NR	35	NR	Effect size Cohen's d=0.20	0.227
	Waite et al, 2019 ¹⁵²	14.7	Internet CBT with accompanying parent sessions for half the group and no parent sessions for the other half, 10 weeks	change from baseline	17	30	59.48 (SD: 14.87)	30	55.18 (SD: 12.48)	Effect size (95% CI) 0.04 (0.00 to 0.18)	NR
	Waite et al, 2019 ¹⁵²	14.7	Internet CBT with accompanying parent sessions for half the group and no parent sessions for the other half, 10 weeks	CAIS-C change from baseline	17	30	18.04 (SD: 16.97)	30	17.59 (SD: 13.09)	Effect size (95% CI) 0.01 (0.00 to 0.12)	NR

Treatment		Mean Age		Outcome		Treatment		Placebo	Placebo Score	Between- Group	Between- Group P
(Condition)	Author, Year	(Years)	Duration	Measure	(Weeks)	N	(SD/SE)	N	(SD/SE)	Difference	Value
Internet CBT (continued)	Waite et al, 2019 ¹⁵²		accompanying parent sessions for half the group and no parent sessions for the other	CAIS-P change from baseline	17	30	23.60 (SD: 21.81)	30	19.63 (SD: 16.34)	Effect size (95% CI) 0.04 (0.00 to 0.19)	NR
Parent- delivered CBT	Thirlwall et al, 2013 ¹⁴⁵	NR, partici-	half, 10 weeks Parent-delivered CBT with a self-help book, 8 weeks	CAIS-P	12	IG2: 41	IG1: 13.97 (SD: 14.64) IG2: 6.39 (SD: 6.29)	48	,	NR IG2 vs. CG:	IG1 vs. CG: P=NS; IG2 vs. CG=0.0045

Abbreviations: CAIS-C=Child Anxiety Impact Scale; CAIS-P=Child Anxiety Impact Scale-Parent; CALIS=Child Anxiety Life Interference Scale; CALIS-C=Child Anxiety Life Interference Scale-Child; CALIS-F=Child Anxiety Life Interference Scale-Father; CALIS-M=Child Anxiety Life Interference Scale-Mother; CBT=cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CI=confidence interval; GAD=general anxiety disorder; IG=intervention group; N=number; NR=not reported; NS=not significant; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; QOL=quality of life; SD=standard deviation; SocAD=social anxiety disorder; vs.=versus; WHO-5=World Health Organization Five Item Well-being Index.

Appendix F Table 11. Anxiety Interventions: Subgroup Analyses for Benefits

Author, Year, Registry Number	Treatment Interventions and Comparators	Qualitative Results
Albano et al, 2018 ²⁰⁵ ; Taylor et al 2018 ²⁰⁶ ;	IG1: Individual child- focused in-person CBT (N=139) IG2: Sertraline (N=133)	At post-treatment, anxiety severity as measured by independent evaluators (PARS) was significantly higher for participants of Hispanic ethnicity receiving CBT. Parent-rated anxiety severity (SCARED-P) was significantly higher for participants of Hispanic ethnicity receiving sertraline.
Sachez et al, 2019 ²⁰⁸ ; Rynn et al, 2015 ²⁰⁹ ;	IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	After accounting for treatment engagement and other demographic factors, there were no statistically significant differences in response, remission, or relapse based on race.
et al, 2015 ²¹⁰ ; Ginsburg et al, 2011 ²¹¹ NCT00052078	CC. Flaceso (N=70)	At post-treatment, parent-reported anxiety-related school impairment (CAIS) was significantly lower among male participants receiving either sertraline or sertraline in combination with CBT. There were no statistically significant sex effects based on youth-reported anxiety-related school impairment (CAIS).
		At post-treatment, age was not a statistically significant moderator of the effect of treatment on any outcome.
		The rate of overall AEs was significantly higher in children than in adolescents who received sertraline. The rate of total psychiatric AEs was significantly higher in children compared with adolescents across all treatment arms. The rate of total physical AEs was not significantly different between children and adolescents.
	IG1: Group child+parent in-person CBT (N=54) CG: Wait-list (N=17)	Age and sex were not significant moderators of clinician's severity ratings (DISCAP) or self-report measures (RCMAS).
	IG1: Individual child- focused in-person CBT (N=148) CG: TAU (N=68)	At post-treatment, age significantly moderated the effect of treatment on response status, indicating that beneficial effects of treatment were strongest for older participants. No moderation effects were observed at 1-year followup.
NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	Age and sex were not significant moderators of GAD severity (PARS).
Pine et al, 2001 ¹²⁴ Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵	IG1: Fluvoxamine (N=63) CG: Placebo (N=65)	Age, sex, and race were not significant moderators of treatment effects on any outcome.
Barrett et al, 1996 ⁷⁰	IG1: Individual child- focused CBT (N=28) IG2: Child+Parent CBT (N=25) CG: Wait-list (N=26)	At post-treamtment and 1-year followup, female and younger (7 to 10 years) participants who received child and parent-focused CBT had significantly higher rates of loss of diagnosis (ADIS) compared with those who received child-focused CBT. There were no significant differences across treament conditions at post-treatment or followup for male or older (11 to 14 years) participants.

Abbreviations: ADIS=Anxiety Disorders Interview Schedule; AE=adverse event; CAIS=Child Anxiety Impact Scale; CBT=cognitive behavioral therapy; CG=control group; DISCAP=Diagnostic Interview Schedule for Children, Adolescents, and Parents; GAD=general anxiety disorder; IG=intervention group; PARS=Pediatric Anxiety Rating Scale; RCMAS=Revised Children's Manifest Anxiety Scale; SCARED-P=Screen for Anxiety Related Emotional Disorders-Parents; TAU=treatment as usual.

Appendix F Table 12. Anxiety Interventions: Suicide-Related Harms for Anxiety Pharmacotherapy Studies (KQ 5)

Treatment (Condition)	Author, Year	Mean Age	Dose (md/day)	Outcome Measure	Time Point (Weeks)	Treatment N		Placebo N	N (%)	Effect Measure (95% CI), P-Value
Duloxetine (GAD)	Strawn et al, 2015 ¹⁴²	12.4	Flexibly dosed duloxetine (30– 120 mg/d)	Suicidal ideation	10	135	1 (1)	137	0 (0)	p=NR
Escitalopram (GAD)	Strawn et al, 2020 ¹⁴³	14.8	Forced titration to 15 mg/d, then	Aborted suicide attempt	8	26	1 (3.8)	25	0 (0)	p=NR
			flexible titration to	Self-injurious behavior	8	26	2 (7.7)	25	1 (4.0)	p=NR
			20 mg/d, 8 weeks	Worsening of suicide- related harms	8	26	6 (23.1)	25	2 (8.0)	p=NR
				Emergence or worsening of suicidality	8	26	NR	25	NR	p=0.449
Sertraline	Walkup et al,	10.7	25 mg/day, up to	Suicidal attempts	12	133	0 (0)	76	0 (0)	p=NR
(GAD,	2008153		200 mg/day by 8th	Suicidal ideation	12	133	0 (0)	76	1 (1.3)	p=NR
separation anxiety disorder, social anxiety disorder)			week, for 12 weeks	Self-harm behavior without suicidal attempt	12	133	1 (0.8)	76	0 (0)	p=NR

Abbreviations: CI=confidence interval; GAD=general anxiety disorder; KQ=key question; N=number; NR=not reported

Appendix F Table 13. Anxiety Interventions: Other Adverse Events for Anxiety Pharmacotherapy Studies (KQ 5)

Treatment (Condition)	Author, Year	Mean Age	Dose (md/day)	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), P-Value
Fluoxetine (Any)	Birmaher et al, 2003 ⁷³	11.8	10 mg/d, after first week, up to 20 mg/d, 12 weeks		12	35	Not calculable (44)	32	Not calculable (22)	p=0.04
				Neurological complaints (headaches, drowsiness),	2	36	16 (44)		5 (14)	p=0.04
				Excitement, giddiness, or disinhibition	12	36	7 (19)	36	4 (11)	p=NS
Fluvoxamine (GAD,	Pine et al, 2001 ¹²⁴	10.4	50 mg/d, then 50 mg/w to max. 300	Abdominal discomfort	8	63	31 (49)	65	18 (28)	p=0.02
separation anxiety disorder, or social anxiety disorder)	Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵		mg/d in adolescents and 250 mg/d in	Headache, increased motor activity, insomnia, nasal congestion, drowsiness, nausea, diarrhea, influenza, or upper respiratory infection	8	63	NR	65	NR	p=NS
Sertraline	Rynn, 2001 ¹³⁰	11.7	25 mg for the first	Dizziness	9	11	2 (18)	11	7 (64.4)	p<0.08
(GAD)			week and 50 mg	Nausea	9	11	Not calculable (5)	11	6 (55)	p<0.06
			for weeks 2 to 9, 9	Stomach pain	9	11	2 (18)	11	7 (64)	p<0.08
			weeks	Dry mouth	9	11	6 (55)	11	3 (27)	p=0.39
				Drowsiness	9	11	8 (73)	11	5 (45)	p=0.39
				Leg spasms	9	11	4 (36)	11	1 (9)	p=0.31
				Restlessness	9	11	6 (55)	11	3 (27)	p=0.39
Duloxetine (GAD)	Strawn et al, 2015 ¹⁴²	12.4	Flexibly dosed duloxetine (30– 120 mg/d)	Treatment- emergent AEs	10	135	106 (78.5)	137	90 (65.7)	p=0.22
Escitalopram (GAD)	Strawn et al, 2020 ¹⁴³	14.8	15 mg/d, then	Bruising	8	26	4 (15)	25	0 (0)	p=0.06
·			flexible titration to 20 mg/d, 8 weeks	Other AEs reported by system organ class	8	26	Varies by outcome	25	Varies by outcome	p=NS

Appendix F Table 13. Anxiety Interventions: Other Adverse Events for Anxiety Pharmacotherapy Studies (KQ 5)

Treatment				Outcome	Time Point	Treatment		Placebo		Effect Measure (95%
(Condition)	Author, Year	Mean Age	Dose (md/day)	Measure	(Weeks)	N	N (%)	N	N (%)	CI), P-Value
	Walkup et al, 2008 ¹⁵³	10.7	25 mg/day, up to 200 mg/day by 8th	Homicidal ideation	12	133	2 (1.5)	76	0 (0)	p=NS
separation anxiety				Homidical attempts	12	133	0 (0)	76	0 (0)	p=NS
disorder, or social anxiety				Any physical AEs	12		,	76	35 (46.1)	p=NS
disorder)				Any psychiatric AEs	12	133	23 (17.3)	76	10 (13.2)	p=NS

Abbreviations: AE=adverse event; CI=confidence interval; GAD=general anxiety disorder; GI=gastrointestinal; KQ=key question; N=number; NR=not reported; NS=not significant.

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	Placebo	Placebo Mean Score (SD)	Difference	Between- Group P Value
Individual in- person youth CBT vs. TAU	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	CDRS-R	52 weeks	106	30.14 (11.26)	106	28.24 (10.54)		P=0.04
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	CDRS-R	104 weeks	106	28.11 (9.88)	106	29.17 (10.79)	-1.30*	P=0.36
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	delivered sessions	CES-D (youth reported)	52 weeks	106	22.59 (7.00)	106	22.51 (7.43)	-2.88*	P<0.005
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	CES-D	104 weeks	106	21.46 (7.44)	106	21.91 (6.95)	-0.32*	P=0.62
	Clarke et al, 2005 ⁷⁶	15.3 (1.6)	5 to 9 therapist delivered sessions (duration not specified)	CES-D	52 weeks	53	11.5 (11.0)	50	14.9 (10.1)	-3.40	p=0.07
	Clarke et al, 2005 ⁷⁶	15.3 (1.6)	5 to 9 therapist delivered sessions (duration not specified)	HAM-D	52 weeks	53	4.9 (7.1)	50	6.5 (6.6)	-1.60	p=0.32
Individual in- person CBT vs. Placebo	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist delivered sessions plus 2 parent-only sessions over 12 weeks	CDRS-R	6 weeks	111	44.63 (8.30)	112	44.90 (7.32)	-0.27	NR
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist delivered sessions plus 2 parent-only sessions over 12 weeks		12 weeks	111	42.06 (9.18)	112	41.77 (7.99)	0.29	P=0.97
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist delivered sessions plus 2 parent-only sessions over 12 weeks		6 weeks	111	69.10 (13.59)	112	69.43 (10.94)		NR
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist delivered sessions plus 2 parent-only sessions over 12 weeks	RADS	12 weeks	111	67.96 (14.18)	112	66.68 (11.41)	1.28	P=0.94

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	N	1 -	Between- Group Difference	Between- Group P Value
	Fristad et al, 2019 ⁹⁰	IG1: 11.7 (2.1) CG: 11.1 (2.4)	Family-based therapy with CBT techniques with parent at beginning and end of session over 12 weeks	CDRS-R	12 weeks	18	30 (9)	18	31 (11)	-1.00	p=0.88
	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping with Depression Course), over 8 weeks plus weekly meetings	BDI	8 weeks	37	10.1 (9.1)	27	16.0 (11.2)		P<0.01
	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping with Depression Course), over 8 weeks plus weekly meetings	HAM-D	8 weeks	37	4.6 (4.8)	27	7.7 (7.0)	-3.10	P=NS
Group in-person CBT + parent sessions vs. wait-list	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping with Depression Course), plus 8 weekly 2-hour parent sessions (6 separate, 2 held jointly with adolescent group) over 8 weeks	BDI	8 weeks	32	13.3 (10.9)		16.0 (11.2)		P<0.01
	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping with Depression Course), plus 8 weekly 2-hour parent sessions (6 separate, 2 held jointly with adolescent group) over 8 weeks	HAM-D	8 weeks	32	6.7 (7.1)	27	7.7 (7.0)	-1.00	P=NS

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	Placebo	Placebo Mean Score (SD)	Between- Group Difference	Between- Group P Value
Internet-based individual CBT vs. attention control	Topooco et al, 2018 ¹⁴⁷	IG1: 17.2 (1.0) CG: 16.9 (1.1)	with 8 skill-based modules plus weekly 30-minute chat sessions with therapist over 8 weeks		8 weeks	33	19.9 (7.2)	37	25.2 (7.8)	-5.30	p<0.05
	2018 ¹⁴⁷	CG: 16.9 (1.1)	with 8 skill-based modules plus weekly 30-minute chat sessions with therapist over 8 weeks	PHQ-9	8 weeks	33	9.7 (2.9)	37	10.8 (3.0)	-1.10	p=NS
	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	BDI-II	8 weeks	35	16.0 (11.3)	35	24.8 (10.4)	-8.80	p<0.001
	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	MFQ	8 weeks	35	24.3 (12.8)	35	31.0 (9.8)	-6.70	p<0.01
Interpersonal psychotherapy vs. TAU	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	BDI	12 weeks	34	8.4 (11.0)	29	12.3 (9.7)	-3.90	p=0.04
	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)		CGI-I	12 weeks	34	2.3 (1.3)	29	3.1 (1.6)	-0.80	p=0.03
	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	CGI-S	12 weeks	34	2.4 (1.3)	29	3.0 (1.4)	-0.60	p=0.03

Treatment		Mean Age	Intervention and	Outcome	Time Point	Treatment	Treatment Mean		Placebo Mean Score	Between- Group	Between- Group P
(Condition)	Author, Year	_	Duration	Measure	(Weeks)	N	Score (SD)			Difference	•
Interpersonal psychotherapy vs. TAU (continued)	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	HAM-D	12 weeks	34	8.7 (8.0)	29	12.8 (8.4)	-4.10	p=0.01
	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	HAM-D	16 weeks	34	6.9 (NR)	29	10.6 (NR)	-3.70	P=0.01
Parent Child Interaction Therapy-Emotion Development (PCIT-ED) vs. wait-list	Luby et al, 2018 ¹¹¹	IG1: 5.1 (1.0) CG: 5.3 (1.1)		EC MDD core score	Change at 18 weeks	114	NR	115		Mean difference (SE) -2.34 (0.26)	p<0.0001
	Luby et al, 2018 ¹¹¹	IG1: 5.1 (1.0) CG: 5.3 (1.1)	Manualized PCIT-ED sessions to teach parent followed by coaching parent-child interactions using a bug-in-the-ear device over 18 weeks		Change at 18 weeks	114	NR	115		Adjusted mean difference (SE) -11.91 (1.29)	p<0.0001

^{*} Across 0 to 52 weeks, not a comparison at 52 weeks.

Abbreviations: BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CES-D=Center for Epidemiological Studies-Depression; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; HAM-D=Hamilton Depression Rating Scale; IG=intervention group; IPT-A=interpersonal psychotherapy for depressed adolescents; K-SADS-EC=Schedule For Affective Disorders And Schizophrenia For School-Age Children-Early Childhood version; MDD=major depressive disorder; MFQ=mood & feelings questionnaire; N=number; NR=not reported; NS=not significant; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PFC=Preschool Feelings Checklist; PHQ-9=Patient Health Questionnaire, 9 question; RADS=Reynolds Adolescent Depression Scale; SD=standard deviation; TAU=treatment as usual; vs.=versus.

Appendix F Table 15. Depression Pharmacotherapy Interventions vs. Placebo: Depression Symptoms

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (md/day)	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	Placebo N	Placebo Mean Score (SD)	Between- Group Difference	Between- Group P Value
Escitalopram vs. placebo	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Change in CDRS-R	8 weeks	129	-22.1 (SEM: 1.22)	132	-18.8 (SEM: 1.27)	-3.3	0.022
·	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Change in CGI-I	8 weeks	129	2.2 (SEM: 0.11)	132	2.6 (SEM: 0.11)	-0.4	0.008
	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	CGI-S	8 weeks	129	-1.8 (SEM: 0.11)	132	-1.4 (SEM: 0.12)	-0.4	0.007
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	Change in CDRS-R	8 weeks	154	-21.9 (NR)	157	-20.2 (NR)	-1.7	0.31
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	Change in CGI-I	8 weeks	154	2.3 (NR)	157	2.5 (NR)	-0.2	0.169
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	Change in CGI-S	8 weeks	154	-1.6 (NR)	157	-1.3 (NR)	-0.3	0.057
Fluoxetine vs. placebo	March, 2004 ¹¹³	14.6 (1.5)		Change in CDRS-R	6 weeks	109	39.8 (7.37)	112	44.9 (7.32)	-5.1	NR
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in CDRS-R	12 weeks	109	36.3 (8.18)	112	41.8 (7.99)	-5.5	0.10
	March, 2004 ¹¹³	14.6 (1.5)		Change in RADS	6 weeks	109	63.4 (12.44)	112	69.4 (10.94)	-6.0	NR
	March, 2004 ¹¹³	14.6 (1.5)		Change in RADS	12 weeks	109	60.6 (13.07)	112	66.7 (11.41)	-6.1	0.34

Abbreviations: CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; IG=intervention group; N=number; NR=not reported; RADS=Reynolds Adolescent Depression Scale; SD=standard deviation; SEM=standard error of the mean; vs.=versus.

Appendix F Table 16. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Depression Symptoms

			_		Time		Treatment		Placebo	Between-	Between-
Treatment		Mean Age	Dose	Outcome	Point	Treatment		Placebo	Score	Group	Group P
(condition)	Author, Year	(SD)	(md/day)	Measure	(Weeks)	N	(SD)	N	(SD/SE)	Difference	Value
Fluoxetine vs.	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	6 weeks	107	38.10 (7.78)	112	44.9 (7.32)	-6.80	NR
placebo	·	, ,	J	CDRS-R			, ,		,		
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	12 weeks	107	33.79 (8.24)	112	41.8 (7.99)	-8.01	P=0.001
				CDRS-R							
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	6 weeks	107	60.90 (11.59)	112	69.4 (10.94)	-8.50	NR
	·	, ,		RADS			, ,		, ,		
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	12 weeks	107	56.95 (12.24)	112	66.7 (11.41)	-9.75	P=0.001
		. ,		RADŠ			. ,		,		

Abbreviations: CDRS-R=Children's Depression Rating Scale-Revised; N=number; NR=not reported; SD=standard deviation; SE=standard error; vs.=versus.

Appendix F Table 17. Depression Collaborative Care Intervention vs. Treatment as Usual: Depression Symptoms

Treatment		Mean	Intervention	Outcome	Time Point	Treatment		Placebo	Placebo Mean Score	Between-Group	Between- Group P
(Condition)	Author, Year	Age (SD)		Measure	(Weeks)	N	(95% CI)	N	(95% CI)	Difference	Value
	Richardson et al, 2014 ¹²⁷	, ,	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months		6 months	50	NR	51		Mean difference between groups (95% CI) -8.5 (-13.4 to -3.6)	P=0.001
	Richardson et al, 2014 ¹²⁷	, ,	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months	CDRS-R	12 months		27.5 (23.8 to 31.1)		38.6)	Mean difference between groups (95% CI) -9.4 (-15.0 to -3.8)	P=0.001

Abbreviations: CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CI=confidence interval; N=number; SD=standard deviation vs.=versus.

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p value
Individual in- person youth CBT vs. TAU	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	MDD response*	52 weeks	106	90 (90.9)	106	87 (87.9)	OR: 1.39 (95% CI, 1.03 to 1.87)
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	MDD Response*	104 weeks	106	93 (93.9)	106	93 (93.9)	OR: 1.38 (95% CI, 1.03 to 1.84)
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	MDD Recovery [†]	52 weeks	106	79 (79.8)	106	68 (68.7)	OR: 1.60 (95% CI, 1.15 to 2.21)
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist delivered sessions (duration not specified)	MDD Recovery [†]	104 weeks	106	88 (88.9)	106	78 (78.8)	OR: 1.59 (95% CI, 1.17 to 2.17)
Individual in- person CBT vs. Placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	15 therapist delivered sessions plus 2 parent- only sessions over 12 weeks	CGI ≥2	12 weeks	111	43.2 (34 to 52)	112	34.8 (26 to 44)	p=0.20
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	15 therapist delivered sessions plus 2 parent- only sessions over 12 weeks	CDRS-R score ≤28	12 weeks	111	14 (16)	112	19 (17)	OR: 0.9 (0.44 to 1.88); P=0.80

Treatment (Condition)	Author, Year		Intervention and Duration	Outcome Measure	(Weeks)	N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p value
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	15 therapist-delivered sessions plus 2 parent- only sessions over 12 weeks	Loss of MDD diagnosis based on K- SADS-P/L	12 weeks	NR	(61.1)	NR	(60.4)	OR: 1.0 (0.52 to 1.77); P=0.89
Family CBT vs. placebo		IG1: 11.7 (2.1) CG: 11.1 (2.4)	Family-based therapy with CBT techniques with parent at beginning and end of session over 12 weeks	CDRS-R score ≤28	12 weeks	18	11 (61)	18	10 (56)	p=NS
Group in- person CBT vs. wait-list	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping With Depression Course), over 8 weeks plus weekly meetings		8 weeks	37	24 (64.9)	27	13 (48.1)	IG1/IG2 vs. CG, 1 tailed P<0.05 Cohen's h=0.38 OR: 2.15 (90% CI, 1.01 to 4.59)
Group in- person CBT + parent sessions vs. wait-list	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Completers	Group CBT (Adolescent Coping With Depression Course), plus 8 weekly 2-hour parent sessions (6 separate, 2 held jointly with adolescent group) over 8 week		8 weeks	32	22 (68.8)	27	13 (48.1)	
Internet-based individual CBT vs. attention control	Topooco et al, 2018 ¹⁴⁷	IG1: 17.2 (1.0) CG: 16.9 (1.1)	Internet-based CBT with 8 skill-based modules plus weekly 30-minute chat sessions with therapist over 8 weeks	BDI-II ≥30% decrease	8 weeks	33	20 (60.6)	37	12 (32.4)	p<0.05
	Topooco et al, 2018 ¹⁴⁷	IG1: 17.2 (1.0) CG: 16.9 (1.1)	Internet-based CBT with 8 skill-based modules plus weekly 30-minute chat sessions with therapist over 8 weeks	BDI-II ≥50% decrease	8 weeks	33	14 (42.4)	37	5 (13.5)	p<0.01

Treatment (Condition)	Author, Year		Intervention and Duration	Outcome Measure	(Weeks)	N	N (%; 95% CI)	N	N (%; 95% CI)	Effect Measure (95% CI), p value
	Topooco et al, 2018 ¹⁴⁷	IG1: 17.2 (1.0) CG: 16.9 (1.1)	Internet-based CBT with 8 skill-based modules plus weekly 30-minute chat sessions with therapist over 8 weeks	diagnosis			20 (71.4)	37	4 (16.0)	p<0.001
		IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	decrease	8 weeks		NR	35	NR	p=0.004
Internet based individual CBT vs. attention control (continued)	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	BDI-II ≥13	8 weeks	35	NR	35	NR	p=0.004
	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	BDI-II ≥10	8 weeks	35	NR	35	NR	p=0.004
	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	significant improvement (2 SD below pre-treatment BDI-II mean)	8 weeks	35	16 (46)	35	4 (11)	p=0.001
	Topooco et al, 2019 ¹⁴⁸	IG1: 17.5 (1.1) CG: 17.5 (1.2)	Internet-based CBT with 8 skill-based modules plus weekly 45-minute chat sessions with therapist over 8 weeks	No longer met MDD criteria	8 weeks	27	15 (56)	26	7 (27)	p=0.03
Interpersonal psychotherapy vs. TAU	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	HAM-D score ≤6	12 weeks	34	17 (50)	29	10 (34)	p=NR
	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	BDI score ≤9	12 weeks	34	25 (74)	29	15 (52)	p=0.048

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	(Weeks)	Treatment N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p value
Parent Child Interaction Therapy- Emotion Development (PCIT-ED) vs. wait-list		CG: 5.3 (1.1)	Manualized PCIT-ED sessions to teach parent followed by coaching parent-child interactions using a bug-in-the-ear device over 18 weeks		Change at 18 weeks	114	NR	115		aOR* (95% CI) CG vs. IG1: 9.52 (8.44 to 10.74); P<0.0001
		CG: 5.3 (1.1)	Manualized PCIT-ED sessions to teach parent followed by coaching parent-child interactions using a bug-in-the-ear device over 18 weeks		Change at 18 weeks	100	68 (75)	91	, ,	aOR (95% CI), CG vs. IG1: 12.15 (5.95 to 24.82); P<0.0001

^{*} Major depression diagnostic response defined as ≥8 weeks below the threshold of 5 or more MD symptoms necessary for full diagnosis but where full recovery has not yet occurred.

Abbreviations: aOR=adjusted odds ratio; BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; CGI=Clinical Global Impressions; CI=confidence interval; IG=intervention group; HAM-D=Hamilton Rating Scale for Depression; IG=intervention group; IPT-A=interpersonal psychotherapy for depressed adolescents; K-SADS-EC=Schedule for Affective Disorders and Schizophrenia for School-Age Children-version; K-SADS-PL=Schedule For Affective Disorders And Schizophrenia For School-Age Children-Present and Lifetime Version; MDD=major depressive disorder; N=number; NR=not reported; NS=not significant; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; SD=standard deviation; TAU=treatment as usual; vs=versus.

[†] Recovery defined as ≥ 8 weeks of no or minimal symptoms (K-SADS Diagnostic Status Rating $\leq 1-2$) and little or no impairment.

[‡] Controlled for baseline characteristics, gender, and baseline externalizing disorder.

Appendix F Table 19. Depression Pharmacotherapy Interventions vs. Placebo for Depression in Children: Remission and Loss of Diagnosis

Treatment	Andh an Vann	M A	Dose	Outcome	Time Point			Placebo	N (%) (\$5% (\$1))	Effect Measure (95%
(Condition)	Author, Year Emslie, 2009 ⁸⁶	Mean Age	(mg/day)	Measure CDRS-R ≤28	(Weeks)	N 154	(%; 95% CI)	N 157	(%; 95% CI)	CI), p Value 0.15
Escitalopram vs. placebo	,	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	CDR3-R ≥20	o weeks	104	64 (41.6)	157	56 (35.7)	0.15
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	CDRS-R ≤28	8 weeks	129	59 (45.7)	132	50 (37.9)	0.32
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	CGI-I ≤2	8 weeks	129	81 (62.8)	132	69 (52.3)	0.14
Fluoxetine vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	CDRS-R score ≤28	12 weeks	109	25 (23)	112	19 (17)	1.5 (0.74 to 2.88); P=0.28
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	CGI-I ≤2	12 weeks	109	60.6 (51 to 70)	112	34.8 (26 to 44)	P=0.001
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Loss of MDD diagnosis based on K- SADS-P/L		NR	78.6%	NR	60.4%	P=0.007

Abbreviations: CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; IG=intervention group; K-SADS-PL=Schedule For Affective Disorders And Schizophrenia For School-Age Children-Present and Lifetime Version; MDD=major depressive disorder; N=number; NR=not reported; vs.=versus.

Appendix F Table 20. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Response, Remission, and Loss of Diagnosis

Treatment (Condition)	Author, Year	Mean Age	Dose (mg/day)	Outcome Measure	Time Point (Weeks)	Treatment N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p Value
Fluoxetine	March et al, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CDRS-R	12 weeks	107	40 (37)	112		3.0 (1.58 to 5.79);
	Curry et al, 2006 ²¹⁷			score ≤28						P=0.0009
	Emslie et al, 2006 ²¹⁸									
	Kennard et al, 2006 ²¹⁹									
	Vitiello et al, 2006 ²²⁰									
	March et al, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CGI-I ≤2	12 weeks	107	71.0 (62	112	34.8 (26 to 44)	P=0.001
	Curry et al, 2006 ²¹⁷						to 80)			
	Emslie et al, 2006 ²¹⁸									
	Kennard et al, 2006 ²¹⁹									
	Vitiello et al, 2006 ²²⁰									
	March et al, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Loss of MDD	12 weeks	NR	85.3%	NR	60.4%	4.1 (2.00 to 8.44);
	Curry et al, 2006 ²¹⁷			diagnosis						P=0.0001
	Emslie et al, 2006 ²¹⁸			based on K-						
	Kennard et al, 2006 ²¹⁹			SADS-P/L						
	Vitiello et al, 2006 ²²⁰									

Abbreviations: CDRS-R=Children's Depression Rating Scale-Revised; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; K-SADS-PL=Schedule for Affective Disorders and Schizophrenia for School-Age Children-present and lifetime version; MDD=major depressive disorder; N=number; NR=not reported; vs.=versus.

Appendix F Table 21. Depression Collaborative Care Intervention vs. Treatment as Usual: Response, Remission, and Loss of Diagnosis

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p Value
Collaborative care vs. enhanced usual care	Richardson et al, 2014 ¹²⁷	15.3 (1.3)	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months	reduction in CDRS-R	6 months	50	NR (48.4*)	51	, ,	OR (95% CI): 3.1 (1.2 to 7.9), P=0.02
	Richardson et al, 2014 ¹²⁷	15.3 (1.3)	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months	≥50% reduction in CDRS-R	12 months	50	NR (67.6*)	51		OR (95% CI): 3.3 (1.4 to 8.2), P=0.009
	Richardson et al, 2014 ¹²⁷	15.3 (1.3)	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months	PHQ-9 <5	6 months	50	NR (36.6*)	51		OR (95% CI): 5.2 (1.6 to 17.3), P=0.007
	Richardson et al, 2014 ¹²⁷	15.3 (1.3)	Choice of treatment (antidepressant, brief CBT, or both), and followup over 12 months	PHQ-9 <5	12 months	50	NR (50.4*)	51		OR (95% CI): 3.9 (1.5 to 10.6), P=0.007

^{*} Imputed % based on 20 multiple imputations.

Abbreviations: CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CI=confidence interval; N=number; NR=not reported; OR=odds ratio; PHQ-9=Patient Health Questionnaire-9; SD=standard deviation; vs.=versus.

Appendix F Table 22. Depression Collaborative Care Intervention vs. Treatment as Usual: Response, Remission, and Loss of Diagnosis

Treatment (Condition)	Author, Year	Mean Age (SD)		Outcome Measure	Time Point (Weeks)	Treatment N	N (%; 95% CI)	Placebo N	N (%; 95% CI)	Between- Group Difference	Between- Group P Value
Collaborative		15.3 (1.3)	Choice of	CIS	6 months	50	NR	51	NR	-4.4 (-8.4 to	p=0.03
	et al, 2014 ¹²⁷		treatment							-0.5)	(A priori
enhanced			(antidepressant,								threshold for
usual care			brief CBT, or both),								secondary
			and followup over								outcomes of
			12 months								P ≤0.01)
	Richardson	15.3 (1.3)	Choice of	CIS	12 months	50	16.3 (13.8 to	51	13.4 (10.8 to	-4.3 (-8.3 to	p=0.04
	et al, 2014 ¹²⁷		treatment				18.8)		15.9)	-0.3)	(A priori
			(antidepressant,								threshold for
			brief CBT, or both),								secondary
			and followup over								outcomes of
			12 months								P ≤0.01)

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; CIS=Columbia Impairment Scale; N=number;=standard deviation; vs.=versus.

Treatment (Condition)	Author, Year		Intervention and Duration	Outcome Measure	Time Point (Weeks)	N	(SD)	N	Placebo Mean Score (SD)	Difference	P value
Individual in- person youth CBT vs. TAU	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist- delivered sessions (duration not specified)	CGAS	52 weeks	106	72.33 (9.97)		74.10 (10.81)	4.2 (95% CI, 1.55 to 6.86)	P<0.007 favoring CBT
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist- delivered sessions (duration not specified)	CGAS	104 weeks	106	76.86 (11.03)	106	76.45 (11.09)	0.13 (95% CI, -2.08 to 2.34)	P=0.21
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist- delivered sessions (duration not specified)	PEDS-QL	52 weeks	106	75.40 (14.57)	106	76.94 (12.43)	0.55 (95% CI, -3.21 to 4.31)	P=0.73
	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	4 to 8 therapist- delivered sessions (duration not specified)	PEDS-QL	104 weeks	106	75.40 (14.57)	106	76.94 (12.43)	1.05 (95% CI, -2.27 to 4.36)	P=0.90
	Clarke et al, 2005 ⁷⁶	15.3 (1.6)	5 to 9 therapist- delivered sessions (duration not specified)	CGAS	52 weeks	53	71.4 (8.7)	50	68.4 (7.6)	NR	P=0.22
	Clarke et al, 2005 ⁷⁶	,	5 to 9 therapist- delivered sessions (duration not specified)	SF-12 MCS	52 weeks	53	45.4 (9.3)		,	NR	P=0.04
	Clarke et al, 2005 ⁷⁶	,	delivered sessions (duration not specified)	SF-12 PCS	52 weeks	53	49.0 (5.8)		- (,	NR	P=0.84
Individual in- person CBT vs. placebo pill	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	CGAS	6 weeks	111	56.7 (9.66)	112	57.0 (9.22)	NR	NR

Treatment (Condition)	Author, Year		Intervention and Duration	Outcome Measure	Time Point (Weeks)	N	(SD)	N	Placebo Mean Score (SD)	Difference	P value
Individual in- person CBT vs. placebo pill (continued)	2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	CGAS	12 weeks	111	60.0 (11.47)		59.3 (12.72)		P=0.3805
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	CGAS	Change at 12 weeks	111	9.7 (12.12)	112	9.9 (12.38)	NR	P=NS
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	HoNOSCA	12 weeks	111	11.7 (6.09)	112	11.2 (6.15)	NR	p=0.3344
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	HoNOSCA	Change in 12 weeks	111	-3.6 (5.58)		-4.2 (5.71)	NR	p=NR
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	PQ-LES-Q	12 weeks	111	47.4 (10.84)	112	48.2 (9.91)	NR	p=0.4630
	March et al, 2004 ¹¹³	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	PQ-LES-Q	Change in 12 weeks	111	4.2 (10.01)	112	5.2 (10.16)	NR	p=NS
Group in- person CBT vs. wait-list		16.2 (1.3) Complet- ers	Group CBT (Adolescent Coping with Depression Course), over 8 weeks plus weekly meetings	GAF	8 weeks	37	71.0 (11.7)	27	64.5 (11.8)	NR	IG1/IG2 vs. CG P<0.05; effect size=0.54

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	Placebo N	Placebo Mean Score (SD)	Between- Group Difference	P value
Group in- person CBT + parent sessions vs. wait-list	Clarke et al, 1999 ⁴⁵	16.2 (1.3) Complet- ers	Group CBT (Adolescent Coping with Depression Course), plus 8 weekly 2-hour parent sessions (6 separate, 2 held jointly with adolescent group) over 8 weeks	GAF	8 weeks	32	69.9 (14.9)	27	64.5 (11.8)	NR	IG1/IG2 vs. CG P<0.05; effect size=0.54
Interpersonal psycho- therapy vs. TAU	Mufson et al, 2004 ¹¹⁸	15.1 (1.9)	Manualized IPT-A during 12 sessions in a 12- to 16-week period	CGAS	12 weeks	34	66.7 (13.0)	29	59.5 (13.5)	NR	p=0.04, effect size 0.54
	Mufson et al, 2004 ¹¹⁸	, ,	Manualized IPT-A during 12 sessions in a 12- to 16-week period		16 weeks	33	NR	29	NR	NR	p=0.06, effect size NR
	2004 ¹¹⁸		sessions in a 12- to 16-week period	Overal	12 weeks	34	2.23 (0.66)			NR	p=0.01, effect size 0.55 Repeated measures ANOVA time x treatment interaction P=0.003
PCIT-ED vs. wait-list	Luby et al, 2018 ¹¹¹	IG1: 5.1 (1.0) CG: 5.3 (1.1)	Manualized PCIT- ED sessions to teach parent followed by coaching parent- child interactions using a bug-in- the-ear device over 18 weeks	CGAS	Change to 18 weeks	114	NR	115		Adjusted* mean difference (SE) 20.5 (2.3)	p<0.0001

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Mean Score (SD)	Placebo N	Placebo Mean Score (SD)	Between- Group Difference	P value
	2018111	(1.0) CG: 5.3 (1.1)	Manualized PCIT- ED sessions to teach parent followed by coaching parent- child interactions using a bug-in- the-ear device over 18 weeks		Change to 18 weeks	114	NR	115		Adjusted mean difference (SE) 3.19 (0.46)	•

^{*} Controlled for baseline characteristics, gender, and baseline externalizing disorder.

Abbreviations: ANOVA=analysis of variance; CAFAS=Child and Adolescent Functional Assessment Scale; CBT=cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CI=confidence interval; GAF=Global Assessment of Functioning; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; IG=intervention group; IPT-A=intensive interpersonal psychotherapy for depressed adolescents; N=number; NR=not reported; NS=not significant; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PFC=Preschool Feelings Checklist; Preschool and Early Childhood Functional Assessment Scale/Child and Adolescent Functional Assessment Scale; PEDS-QL= Pediatric Quality of Life Inventory; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; SAS-SR=Social Adjustment Scale—Self-Report; SD=standard deviation; SE=standard error; SF-12 MCS=Short-Form 12 Mental Component Score; SF-12 PCS=Short-Form 12 Physical Component Score; TAU=treatment as usual; vs.=versus.

Appendix F Table 24. Depression Psychotherapy vs. Placebo: Functioning (Categorical)

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)		N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p Value
Individual in- person CBT vs. placebo pill	,		15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	C-GAS >70	12 weeks	111	15 (13.5)	112	21 (18.7)	P=NS

Abbreviations: CBT=cognitive behavioral therapy; CGAS=Children's Global Assessment Scale; CI=confidence interval; N=number; NS=not significant; SD=standard deviation; vs.=versus.

Appendix F Table 25. Depression Pharmacotherapy Interventions vs. Placebo: Functioning (Continuous)

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Escitalopram vs. placebo	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Change in CGAS	8 weeks	154	14.9 (SE: 1.11)	157	12.7 (SE: 1.15)	LSMD=2.169 (-0.439 to 4.777)	0.103
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg	Change in CGAS	8 weeks	129	15.6	132	12.7	2.9	0.065
Fluoxetine vs. placebo	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CGAS	6 weeks	109	59.9 (SD: `10.58)	112	57.0 (SD: 9.22)	2.9	NR
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CGAS	12 weeks	109	62.1 (SD: 11.91)	112	59.3 (SD: 12.72)	2.8	P=0.0381
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in CGAS	12 weeks	109	12.6 (SD: 12.31)	112	9.9 (SD: 12.38)	2.7	P=NS
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	HoNOSCA	12 weeks	109	10.9 (SD: 6.35)	112	11.2 (SD: 6.15)	-0.3	P=0.3344
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in HoNOSCA	12 weeks	109	-5.1 (SD: 5.74)	112	-4.2 (SD: 5.71)	-0.9	P=NS
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	PQ-LES-Q	12 weeks	109	51.2 (SD: 10.43)	112	48.2 (SD: 9.91)	3.0	0.7215
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in PQ-LES-Q	12 weeks	109	6.6 (SD: 10.23)	112	5.2 (SD: 10.16)	1.4	P=NS

Abbreviations: CG=control group; CGAS=Children's Global Assessment Scale; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; IG=intervention group; LSMD=least-square mean difference; NR=not reported; NS=not significant; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; SD=standard deviation; SE=standard error; vs.=versus.

Appendix F Table 26. Depression Pharmacotherapy Intervention vs. Placebo: Functioning (Categorical)

Trootmont	Author, Year	Moon Ago	Dose (ma/dev)		Time Point (Weeks)	Treatme nt N	N (%; 95% CI)	Placebo N	N (9/ + 059/ CI)	Effect Measure (95% CI), p Value
Treatment	Author, rear	Wean Age	Dose (mg/day)	Measure	(vveeks)	III IN	(%, 95% CI)	IN	(%, 95% CI)	(95% Ci), p value
Fluoxetine	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Rate of	12 weeks	109	22 (20.2)	112	21 (18.7)	P=NS
vs. placebo				nonimpaired						
				patients (C-						
				GAS >70)						

Abbreviations: CGAS=Children's Global Assessment Scale; CI=confidence interval; N=number; NS=not significant; vs.=versus.

Appendix F Table 27. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Functioning (Continuous)

					Time				Placebo	Between-	Between-
		Mean Age	Dose	Outcome	Point	Treatment	Treatment	Placebo	Score	Group	Group P
Treatment	Author, Year	(SD)	(mg/day)	Measure	(Weeks)	N	Score (SD)	N	(SD/SE)	Difference	Value
Fluoxetine	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CGAS	6 weeks	107	62.4 (11.2)	112	57.0 (9.22)	5.4	NR
+ CBT vs.	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	CGAS	12 weeks	107	66.6 (11.91)	112	59.3 (12.72)	7.3	P<0.0001
placebo	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	12 weeks	107	16.7 (12.31)	112	9.9 (12.38)	6.8	P<0.0001
				CGAS							
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	HoNOSCA	12 weeks	107	9.5 (5.97)	112	11.2 (6.15)	-1.7	P=0.0393
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	12 weeks	107	-6.3 (5.69)	112	-4.2 (5.71)	-2.1	P<0.01
				HoNOSCA							
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	PQ-LES-Q	12 weeks	107	54.7 (11.21)	112	48.2 (9.91)	6.5	P<0.0001
	March, 2004 ¹¹³	14.6 (1.5)	10 to 40 mg	Change in	12 weeks	107	9.6 (10.14)	112	5.2 (10.16)	4.4	p<0.0001
				PQ-LĔS-Q							1-

Abbreviations: CBT=cognitive behavioral therapy; CGAS=Children's Global Assessment Scale; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; N=number; NR=not reported; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; SD=standard deviation; SE=standard error; vs.=versus.

Appendix F Table 28. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Functioning (Categorical)

Treatment	Author, Year	Mean Age	Dose (mg/day)	Outcome Measure	Time Point (Weeks)		N (%; 95% CI)	Placebo N	N (%; 95% CI)	Effect Measure (95% CI), p Value
Fluoxetine + CBT vs. placebo	March, 2004 ¹¹³	14.6 (1.5)		Rate of nonimpaired patients (C-GAS >70)	12 weeks	107	37 (34.6)	112	19 (17)	P=0.009

Abbreviations: CBT=cognitive behavioral therapy; CGAS=Children's Global Assessment Scale; CI=confidence interval; N=number; vs.=versus.

Appendix F Table 29. Depression Interventions: Subgroup Analyses for Benefits

Author, Year, Registry Number	Treatment Interventions and Comparators	Qualitative Results
	IG1: Child-focused Group CBT (N=45) IG2: Child + Parent Group CBT (N=42) CG: Wait-list (N=36)	At posttreatment, sex was not a significant moderator of recovery rates.
Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	(N=107) IG2: Fluoxetine (N=109) IG3: Child + Parent	At posttreatment, age was significant moderator of clinician-rated symptom severity (CDRS-R), indicating adolescents younger than 16 years of age improved more than adolescents who were 16 or older across treatment conditions. At posttreatment, age, gender, and race/ethnicity were not significant moderators of clinician-rated (CGAS, HoNOSCA) and self-reported (PQ-LES-Q) functioning.
	(N=132)	At posttreatment, age significantly moderated the effect of treatment on clinician-rated symptom severity (CGI-S), symptom improvement (CGI-I), and overall functioning (CGAS), indicating that treatment was effective in adolescents (12 to 17 years) but not in children (6 to 11 years).

Abbreviations: CBT=cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CGI-I=Clinical Global Impressions-Improvement; IG=intervention group; N=number; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire.

Appendix F Table 30. Depression Psychotherapy Interventions vs. Placebo: Suicide-Related Outcomes (Continuous)

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point	Treatment N	Treatment Score (SD)	Placebo N	Placebo Score (SD/SE)	Between- Group P Value
	March et al, 2004 ¹¹³	` ,			6 weeks	111	13.18 (11.34)	112	16.85 (11.70)	NR
l.	Curry et al, 2006 ²¹⁷		delivered sessions							
placebo	Emslie et al, 2006 ²¹⁸		plus 2 parent-only							
	Kennard et al, 2006 ²¹⁹		sessions over 12							
	Vitiello et al, 2006 ²²⁰		weeks							
	March et al, 2004113	14.6 (1.5)	15 therapist-	SIQ-Jr	12 weeks	111	11.40 (10.44)	112	15.01 (11.05)	P=0.76
	Curry et al, 2006 ²¹⁷		delivered sessions							
	Emslie et al, 2006 ²¹⁸		plus 2 parent-only							
	Kennard et al, 2006 ²¹⁹		sessions over 12							
	Vitiello et al, 2006 220		weeks							

Abbreviations: CBT=cognitive behavioral therapy; N=number; NR=not reported; SD=standard deviation; SE=standard error; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; vs.=versus.

Appendix F Table 31. Depression Psychotherapy Interventions vs. Treatment as Usual or Placebo: Suicide-Related Outcomes (Categorical)

Treatment (Condition)	Author, Year	Mean Age (SD)		Outcome Measure	Time Point	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Individual in- person youth CBT vs. TAU	Clarke et al, 2016 ⁷⁵	14.6 (1.7)	' '		52 weeks	106	5 (5.8)	106	2 (2.4)	RR: 2.50 (0.50 to 12.60)
	Clarke et al, 2016 ⁷⁵	, ,	delivered sessions (duration not	Suicidal behavior assessed by K-SADS interview	104 weeks	106	1 (1.1)	106		RR: 1.00 (0.06 to 15.78)
Individual in- person CBT vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	delivered sessions plus 2 parent-only sessions over 12 weeks		12 weeks	111	5 (4.50)	112	Also reported	RR: 1.26 (0.35 to 4.57) RR: 1.68 (0.41 to 6.87)
Individual in- person CBT vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	Suicide attempts	12 weeks	111	1 (0.90%)		0 (0)	NR

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CI=confidence interval; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children; N=number; NR=not reported; RR=relative risk; SD=standard deviation; TAU=treatment as usual; vs.=versus.

Appendix F Table 32. Depression Pharmacotherapy Interventions vs. Placebo: Suicide-Related Outcomes (Continuous)

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point	Treatment N	Treatment Score (SD)	Placebo N	Placebo Score (SD/SE)	Difference	
Escitalopram vs. placebo	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Change in SIQ-Jr	8 weeks	155	-4.6 (SEM, 12.0)	157	-2.9 (10.2)	-1.7	0.29
·	Emslie, 200986	IG1: 14.7 (1.6) CG: 14.5 (1.5)	_	Change in MC-SSRS (worsening suicidal behavior)	8 weeks	155	2 (SEM, 1.5)	157	3 (2.3)		NR
		IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Change in MC-SSRS (increase in suicidal ideation)	8 weeks	155	12 (SEM, 9.4)	157	12 (9.2)	0	NR
Fluoxetine vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹	14.6 (1.5)	10 to 40 mg	Change in SIQ-Jr	6 weeks	109	16.20 (12.42)	112	16.85 (11.70)	-0.65	NR
	Vitiello et al, 2006 ²²⁰										
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Change in SIQ-Jr	12 weeks	109	14.44 (11.13)	112	15.01 (11.05)	-0.57	0.36*

^{*} Means adjusted for both fixed (treatment and time) and random (participant and site) effects derived from linear random coefficient model.

Abbreviations: CG=placebo group; CI=confidence interval; IG1=active drug group; MC-SSRS= Modified Columbia Suicide Severity Rating Scale; N=number; SD=standard deviation; SE=standard error; SEM=standard error of the mean; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; vs.=versus.

Appendix F Table 33. Depression Pharmacotherapy Interventions vs. Placebo: Suicide-Related Outcomes (Categorical)

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Escitalopram vs. placebo	Emslie, 2009 86	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Self-harm related AE (other than suicidality)	8 weeks	155	6 (3.9)	157		NR
	Wagner, 2006	12.3 (3.0)	10 to 20 mg	Potential suicide-related events	8 weeks	131	1 (7.8)	133	2 (1.5)	NR
Fluoxetine vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Suicide-related AEs determined by Columbia Classification Algorithm	12 weeks		9 (8.26) ¹¹³ Also reported as 10 (9.2) ²¹⁸			RR: 2.31 (0.73 to 7.29) RR: 3.43 (0.97 to 12.11)
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Suicide attempts	12 weeks	109	2 (1.83)	112	0 (0)	NR

Abbreviations: AE=adverse event; CG=placebo group; CI=confidence interval; IG1=active drug group; N=number; NR=not reported; RR=relative risk; SD=standard deviation; vs.=versus.

Appendix F Table 34. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Suicide-Related Outcomes (Continuous)

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point	Treatment N	Treatment Score (SD/SE)	Placebo N	Placebo Score (SD/SE)	Between- Group Difference	Between- Group P Value
Fluoxetine + CBT vs placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Change in SIQ-Jr	6 weeks	107	14.31 (12.58)	112	16.85 (11.70)	-0.65	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Change in SIQ-Jr	12 weeks		11.79 (11.69)	112	15.01 (11.05)	-0.57	0.02*

^{*} Supplemental between-group comparisons of means at 12 weeks; P=NS.

Abbreviations: CBT=cognitive behavioral therapy; N=number; NS=not significant; SD=standard deviation; SE=standard error; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; vs.=versus.

Appendix F Table 35. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Suicide-Related Outcomes (Categorical)

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Fluoxetine + CBT vs placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Suicide-related AEs determined by Columbia Classification Algorithm	12 weeks		6 (5.61) ¹¹³ Also reported as 5 (4.7) ²¹⁸		Also reported as 3 (2.7) ²¹⁸	RR (95% CI): IG vs. CG: 1.57 (0.46 to 5.41) RR (95% CI): IG vs. CG: 1.75 (0.43 to 7.12)
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Suicide attempts	12 weeks	107	4 (3.7%)	112	0 (0)	NR

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; IG=intervention group; N=number; NR=not reported; RR=relative risk; SD=standard deviation; vs.=versus.

Appendix F Table 36. Depression Psychotherapy vs. Placebo Intervention: Adverse Events and Serious Adverse Events

Treatment (Condition)	Author, Year	Mean Age (SD)	Intervention and Duration	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Effect Measure (95% CI), p Value
Individual in- person CBT vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	delivered sessions plus 2 parent-only sessions over 12	Physical AEs requiring medical attention or causing dysfunction	12 weeks	111	9 (8.1)	112	34 (30.4)	NR
		14.6 (1.5)	15 therapist- delivered	Any psychiatric- related AEs	12 weeks	111	1 (1)	112	9 (9.8)	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	15 therapist- delivered sessions plus 2 parent-only sessions over 12 weeks	Serious AEs	12 weeks	111	5 (4.50)	112	6 (5.36)	OR (95% CI): 0.8 (0.25 to 2.81)
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	delivered	Serious psychiatric- related AEs	12 weeks	111	0 (0)	112	1 (0.89), mania	NR

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CI=confidence interval; N=number; NR=not reported; OR=odds ratio; SD=standard deviation; vs.=versus.

Appendix F Table 37. Depression Pharmacotherapy Interventions vs. Placebo: Adverse Events and Serious Adverse Events

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point (Weeks)	Treatment N	N (%)	Placebo N	N (%)	Between-Group P Value
Escitalopram vs. placebo	Emslie, 2009 ⁸⁶	IG1: 14.7 (1.6) CG: 14.5 (1.5)	10 to 20 mg	Total AEs	8 weeks	155	121 (78.1)	157	118 (75.2)	NR
		IG1: 14.7 (1.6) CG: 14.5 (1.5)	_		8 weeks		4 (2.6), 1 sexual assault, 1 self- injurious behavior, 1 suicidal ideation, 1 irritability		2 (1.3) (1 suicidal tendency, 1 aggravated depression)	NR
	Wagner, 2006 ¹⁵¹	12.3 (3.0)	10 to 20 mg		8 weeks	131	90 (68.7)	133	90 (67.7)	p=0.90
Fluoxetine vs. placebo	Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Physical AEs requiring medical attention or causing dysfunction	12 weeks	109	35 (32.1)	112	34 (30.4)	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Any psychiatric -related AEs	12 weeks	109	20 (21.0)	112	9 (9.8)	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	SAEs	12 weeks	109	13 (11.93)	112	6 (5.36)	OR (95% CI): 2.4 (0.87 to 6.54)
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Serious psychiatric -related AEs	12 weeks	109	1 (0.92), worsening depression	112	1 (0.89), mania	NR

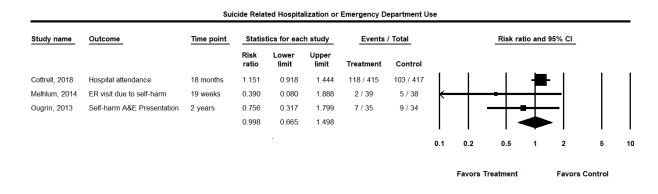
Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CI=confidence interval; N=number; NR=not reported; OR=odds ratio; SAE=serious adverse event; SD=standard deviation; vs.=versus.

Appendix F Table 38. Depression Pharmacotherapy + Psychotherapy Intervention vs. Placebo: Adverse Events and Serious Adverse Events

Treatment (Condition)	Author, Year	Mean Age (SD)	Dose (mg/day)	Outcome Measure	Time Point (Weeks)	Treatment N	Treatment Score (SD)	Placebo N	Placebo Score (SD/SE)	Between- Group P Value
Fluoxetine + CBT vs. placebo	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Physical AEs requiring medical attention or causing dysfunction	12 weeks	107	37 (34.5)	112	34 (30.4)	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Any psychiatric- related AEs	12 weeks	107	12 (15)	112	9 (9.8)	NR
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	SAEs	12 weeks	107	9 (8.41)	112	6 (5.36)	OR (95% CI): 1.6 (0.56 to 4.72)
	March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰	14.6 (1.5)	10 to 40 mg	Serious psychiatric- related AEs	12 weeks		,	112	1 (0.89), mania	NR

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CI=confidence interval; N=number; NR=not reported; OR=odds ratio; SD=standard deviation; SE=standard error; vs.=versus.

Appendix G Figure 1. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Suicide-Related Hospitalization or Emergency Department Use



I-squared: 21.12; p=0.28

Abbreviations: A&E=accident and emergency; CI=confidence interval; ER=emergency room; vs. versus.

Appendix G Figure 2. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Mean Number of Self-Harm Events

Mean Number of Self-harm Events

Study name	Outcome	Time point	Statistics for each study				Sampl	le size		Difference			
			Difference in means	Lower limit	Upper limit	p-Value	Treated	Control					
Cottrell, 2018	Mean Number of Self-harm Events	12 to 18 months	-0.200	-0.574	0.174	0.295	415	417				1	
Mehlum, 2016	Mean Number of Self-harm Events	19 weeks	-13.500	-26.782	-0.218	0.046	39	38	-		-		
Wood, 2001	Mean Number of Self-harm Events	7 months	-1.200	-2.373	-0.027	0.045	32	31					
			-0.762	-2.154	0.631	0.283					•		
									-28.00	-14.00	0.00	14.00	28.00
										Favors Treatment		Favors Control	

I-squared: 68.39; p=0.042

Abbreviations: CI=confidence interval; vs. versus.

Appendix G Figure 3. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Proportion With Self-Harm Events

Number of Self-harm Events Events / Total Odds ratio and 95% CI Study name Outcome Time point Statistics for each study Odds Lower limit p-Value Treatment Cottrell, 2018 Deliberate self-harm 12 to 18 months 1.312 0.875 1.967 0.190 202 / 268 147 / 210 Green, 2011 Self-harm resulting in injury 12 months 0.497 0.045 5.533 0.570 1 / 180 2 / 180 Hazell, 2009 0.871 11.214 0.080 30 / 34 24 / 34 Repetition of self-harm 6 to 12 months 3.125 Rossouw, 2012 Deliberate self-harm 0.095 0.020 0.461 0.003 22 / 36 33 / 35 Wood, 2001 Repeating self-harm 0.140 0.028 0.706 0.017 2/32 10 / 31 7 months 0.549 0.158 1.903 0.345 0.2 0.5 **Favors Treatment Favors Control**

I-squared: 79.14; p=0.001

Abbreviations: CI=confidence interval; vs. versus.

Appendix G Figure 4. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Suicide Symptoms (Beck Hopelessness Scale)

Suicide Treatment on BHS Sample size Difference in means and 95% CI Study name Statistics for each study Outcome Time point Difference in means Lower limit Upper limit p-Value Control King, 2009 BHS -0.980 -2.110 0.150 0.089 223 225 King, 2015 BHS 2 months -2.980 -6.130 0.170 0.064 24 22 Melhlum, 2014 BHS 19 weeks -2.830 -5.859 0.199 0.067 39 38 Tang, 2009 BHS -4.680 -8.145 -1.215 0.008 35 38 6 weeks -2.354 -4.060 -0.648 0.007 10.00 -10.00 Favors Treatment Favors Control

I-squared: 45.98; p=0.135

Abbreviations: BHS=Beck Hopelessness Scale; CI=confidence interval; vs. versus.

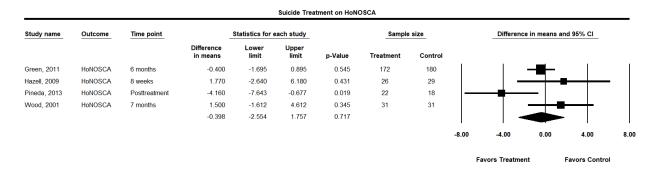
Appendix G Figure 5. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Suicide Symptoms (Suicidal Ideation Questionnaire or Suicidal Ideation Questionnaire-Junior)

Suicide Treatment on SIQ or SIQ-JR Statistics for each study Sample size Std diff in means and 95% CI Study name Outcome Time point Lower Std diff Upper limit p-Value Treatment Control in means Diamond, 2010 SIQ-JR -1.295 -0.291 0.002 35 12 weeks -0.793 31 Green. 2011 SIQ 6 months 0.002 -0.208 0.211 0.987 171 179 -0.060 0.799 37 Hazell, 2009 SIQ 8 weeks -0.526 0.405 34 King, 2009 SIQ-JR 6 weeks -0.195 -0.380 -0.009 0.040 223 225 King, 2015 SIQ-JR 2 months -0.163 -0.742 0.417 0.583 22 Melhlum, 2014 SIQ-JR -0.374 38 37 71 weeks -0.830 0.083 0.109 0.569 Wood, 2001 SIQ 7 months 0.154 -0.375 0.683 28 27 -0.176 -0.361 0.008 0.061 1.00 2.00 -2.00 -1.00 **Favors Treatment Favors Control**

I-squared: 44.80; p=0.092

Abbreviations: CI=confidence interval; SIQ=Suicidal Ideation Questionnaire; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; vs. versus.

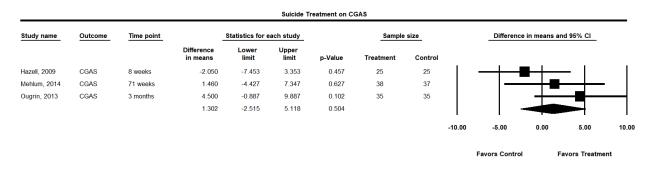
Appendix G Figure 6. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Functional Status (Health of the Nation Outcome Scales for Children and Adolescents)



I-squared: 56.13; p=0.08

Abbreviations: CI=confidence interval; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; vs. versus.

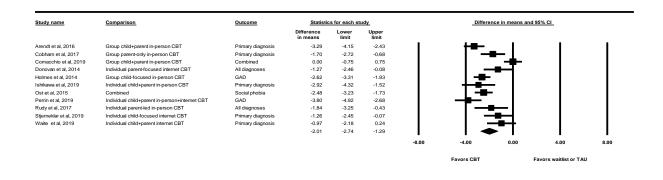
Appendix G Figure 7. Suicide Risk Interventions vs. Treatment as Usual or Attention Control: Functional Status (Clinical Global Assessment Scale)



I-squared: 29.46; p=0.24

Abbreviations: CGAS=Children's Global Assessment Scale; CI=confidence interval; vs. versus.

Appendix G Figure 8. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (ADIS-Clinician Severity Ratings)



Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; GAD=general anxiety disorder; TAU=treatment as usual; vs. versus.

Appendix G Figure 9. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Clinical Global Impressions-Severity)

Study name	<u>Comparison</u>	Statistics for each study				Difference in means and 95% CI				
		Difference in means	Lower limit	Upper limit						
Ginsburg et al, 2020	Individual child-focused in-person CBT	-0.18	-0.58	0.22					- 1	
Rudy et al, 2017	Individual parent-led in-person CBT	-1.33	-2.01	-0.65		-	█-			
Walkup et al, 2008	Individual child-focused in-person CBT	-0.50	-0.87	-0.13						
		-0.60	-1.14	-0.06	ı		lack			
					-8.00	-4.00	0.00	4.00	8.00	
						Favors CBT		avors TAU/place	aho	

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; TAU=treatment as usual; vs. versus.

Appendix G Figure 10. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Multidimensional Anxiety Scale)

Study name	Comparison	Statistic	cs for each stu	ıdy		Difference	e in means a	and 95% CI	
		Difference in means	Lower limit	Upper limit					
Albano et al., 2018	Individual child-focused in-person CBT	-2.00	-5.05	1.05		-			
Ost et al, 2015	Combined	-15.20	-25.44	-4.96	-	-			
/illabo et al, 2018	Combined	-3.25	-7.63	1.14					
		-4.66	-9.66	0.34					
					-16.00	-8.00	0.00	8.00	16.00
						Favors CBT		Favors waitlis	st

Appendix G Figure 11. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Revised Children's Manifest Anxiety Scale)

Study name	Comparison	Statistic	cs for each stu	ıdy		Difference	in means a	and 95% CI	
		Difference in means	Lower limit	Upper limit					
Barrett et al, 1996	Combined	-3.80	-7.10	-0.50	I —	-	— I		- 1
Lyneham et al, 2006	Combined	-5.78	-9.81	-1.76	←	-			
Shortt et al, 2001	Group child+parent in-person CBT	-1.20	-1.96	-0.44			█╾┃		
		-3.08	-5.91	-0.24			-		ı
					-8.00	-4.00	0.00	4.00	8.0
						Favors CBT		Favors waitlis	t

Appendix G Figure 12. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Social Phobia and Anxiety Inventory for Children)

Study name	Comparison	Statistic	s for each	study		Std diff i	n means ar	nd 95% CI	
		Std diff in means	Lower limit	Upper limit					
Asbrand et al, 2020	Group child-focused in-person CBT	-0.59	-1.08	-0.10	- 1				
Ost et al, 2015	Combined	-0.74	-1.40	-0.07					
Sanchez-Garcia et al, 2009	Combined	-2.63	-3.36	-1.89		-■			
Salzer et al, 2018	Individual child-focused in-person CBT	-0.75	-1.22	-0.28					
		-1.14	-1.94	-0.35			◆		
					-8.00	-4.00	0.00	4.00	8.00
						Favors CBT		Favors waitlis	t

Appendix G Figure 13. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Spence Children's Anxiety Scale-Child Rating)

Study name	Comparison	Statistic	s for each st	udy		Difference	in means	and 95% CI	
		Difference in means	Lower limit	Upper limit					
Arendt et al, 2016	Group child+parent in-person CBT	-10.98	-16.62	-5.34	- 1	—	- 1	1	
Cobham et al, 2017	Group parent-only in-person CBT	-7.70	-14.10	-1.30		+=			
Holmes et al, 2014	Group child-focused in-person CBT	-5.96	-19.10	7.18			_	- 1	
shikawa et al, 2019	Individual child+parent in-person CBT	-7.67	-18.09	2.75			-	1	
au et al, 2010	Group child+parent in-person CBT	-14.20	-21.28	-7.12	-	—■—			
yneham et al, 2006	Combined	-11.60	-22.40	-0.79	-		—		
Stjerneklar et al, 2019	Individual child-focused internet CBT	-8.31	-17.23	0.61			→		
hirlwall et al, 2013	Combined	-0.17	-6.68	6.35		-		-	
Vaite et al, 2019	Individual child+parent internet CBT	-3.11	-11.82	5.60			-	-	
		-7.81	-10.99	-4.63			.		
					-24.00	-12.00	0.00	12.00	24.0
						Favors CBT		Favors waitlist	

Appendix G Figure 14. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Anxiety Symptoms (Spence Children's Anxiety Scale-Parent Rating)

Study name	Comparison	Outcome	Statistic	s for each s	tudy		Difference	in means	and 95% CI	
			Difference in means	Lower limit	Upper limit					
Arendt et al, 2016	Group child+parent in-person CBT	Combined	-11.93	-17.55	-6.31	- 1	-		1	- 1
Cobham et al, 2017	Group parent-only in-person CBT	Combined	-10.70	-16.90	-4.50			-		
Holmes et al, 2014	Group child-focused in-person CBT	SCAS-Parent	-1.53	-8.60	5.54		-		-	
shikawa et al, 2019	Individual child+parent in-person CBT	SCAS-Parent	-2.15	-9.34	5.04		-	╼┼	-	
au et al, 2010	Group child+parent in-person CBT	SCAS-Parent	-7.70	-13.93	-1.47		+=	—		
yneham et al, 2006	Combined	Combined	-12.72	-21.49	-3.95	l –	_	-		
Stjerneklar et al, 2019	Individual child-focused internet CBT	Combined	-8.19	-16.22	-0.16					
hirlwall et al, 2013	Combined	SCAS-Parent	-1.85	-6.84	3.15		-	╼┼╴		
Vaite et al, 2019	Individual child+parent internet CBT	SCAS-Parent	4.19	-5.41	13.79			\dashv	-	
			-6.06	-9.57	-2.56			▶		
						-24.00	-12.00	0.00	12.00	24.00
							Favors CBT		Favors waitlis	t

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; SCAS-Parent=Spence Children's Anxiety Scale-Parent-rated; vs. versus.

Appendix G Figure 15. Anxiety Pharmacotherapy Interventions vs. Placebo: Anxiety Symptoms (Clinical Global Impressions-Severity)

etine		Lower limit -2.00	Upper limit -1.00	Pharmacotherapy	Placebo	ı	1			
etine			-1.00	11	11	1	1			
	-0.50	0.70						╋		
		-0.78	-0.22	135	133					
lopram	-0.80	-0.94	-0.66	26	25					
line	-0.80	-1.18	-0.42	133	76					
	-0.84	-1.13	-0.55	305	245			♦		
						-8.00	-4.00	0.00	4.00	8.00
li	ne						-0.84 -1.13 -0.55 305 245 -8.00	-0.84 -1.13 -0.55 305 245 -8.00 -4.00	-0.84 -1.13 -0.55 305 245	-0.84 -1.13 -0.55 305 245

Abbreviation: CI=confidence interval; vs. versus.

Appendix G Figure 16. Anxiety Pharmacotherapy Interventions vs. Placebo: Anxiety Symptoms (Pediatric Anxiety Rating Scale)

Study name		Statistics	for each s	study	Sample siz	<u>e</u>		Differenc	e in means	and 95% CI	
		Difference in means	Lower limit	Upper limit	Pharmacotherapy	Placebo					
Birmaher et al, 2003	Fluoxetine	-2.20	-4.65	0.25	37	37	1	+-	\mapsto		
Pine et al, 2001	Fluvoxamine	-6.90	-9.08	-4.72	61	63	⊬■	-			
Strawn et al, 2015	Duloxetine	-2.80	-4.19	-1.41	135	133			-		
Strawn et al, 2020	Escitalopram	-5.13	-5.79	-4.47	26	25					
Walkup et al, 2008	Sertraline	-2.80	-4.56	-1.04	133	76		+=	-		
		-4.00	-5.54	-2.46	392	334		*			
							-8.00	-4.00	0.00	4.00	8
							Favo	ors pharmacothe	erapy	Favors placebo	

Abbreviation: CI=confidence interval; vs. versus.

Appendix G Figure 17. Anxiety CBT Interventions vs. Treatment as Usual: Response (Clinical Global Impressions-Improvements Scores ≤2)

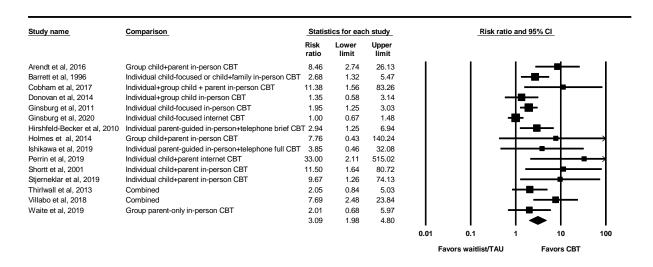
Study name	Comparison	Statis	tics for eac	h study	Events	/ Total		Risk rat	io and 959	% CI	
		Risk ratio	Lower limit	Upper limit	СВТ	Waitlist					
Cornacchio et al, 2019	Group child+parent in-person CBT	16.00	1.00	256.54	7/14	0 / 15			—		
Ginsburg et al, 2020	Individual child-focused in-person CBT	1.15	0.80	1.65	62 / 148	25 / 68					
Hirshfeld-Becker et al, 2010	Individual child+parent in-person CBT	1.97	1.06	3.63	20 / 34	9/30				-	
Rudy et al, 2017	Individual parent-led in-person CBT	17.76	1.17	269.93	10 / 12	0/10			I—	-	\longrightarrow
Valkup et al, 2008	Individual child-focused in-person CBT	2.52	1.65	3.86	83 / 139	18 / 76				-	
Vaite et al, 2019	Individual parent-led in-person CBT	1.33	0.66	2.69	12/30	9/30			╼-		
		1.89	1.17	3.05	194 / 377	61 / 229					
							0.01	0.1	1	10	100
							Fav	ors waitlist/T AU/placebo		Favors CBT	

Abbreviation: CI=confidence interval; TAU=treatment as usual; vs. versus.

Appendix G Figure 18. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Remission (Clinically Significant Change in Spence Children's Anxiety Scale)

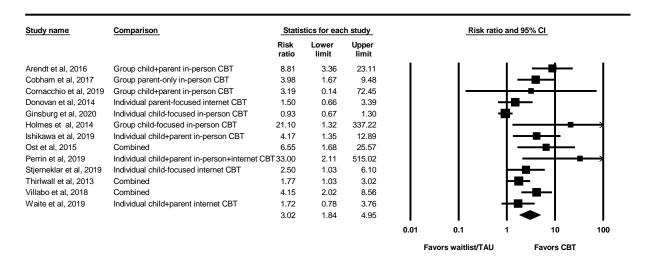
Study name	Comparison	Statis	tics for eac	h study		Risk ra	tio and 9	5% CI	
		Risk ratio	Lower limit	Upper limit					
Arendt et al, 2016	Group child+parent in-person CBT	3.80	1.68	8.56		1	1 -	■-	1
Ishikawa et al, 2019	Individual child+parent in-person Cl	BT1.49	0.80	2.78			+=-		
Lyneham et al, 2006	Combined	2.44	1.06	5.64				⊢	
Stjerneklar et al, 2019	Individual child-focused internet CB	8T 7.33	1.73	31.17			-	-	
		2.68	1.48	4.88					
					0.01	0.1	1	10	100
						Favors waitlist		Favors CBT	

Appendix G Figure 19. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Loss of All Anxiety Diagnoses



Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; TAU=treatment as usual; vs. versus.

Appendix G Figure 20. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Loss of Primary Anxiety Diagnosis



Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; TAU=treatment as usual; vs. versus.

Appendix G Figure 21. Anxiety Pharmacotherapy Interventions vs. Placebo: Response (Clinical Global Impressions-Improvements Scores ≤2)

Study name	Comparison	Statist	ics for eac	ch study	Events / To	tal		Risk ra	tio and 9	5% CI	
		Risk ratio	Lower limit	Upper limit	Pharmacotherapy	Placebo					
Birmaher et al, 2003	Fluoxetine	1.74	1.04	2.89	22 / 36	13 / 37					1
Black et al, 1994	Fluoxetine	1.13	0.38	3.32	3/6	4/9		-		.	
Rynn et al, 2001	Sertraline	10.00	1.53	65.41	10 / 11	1 / 11			-		— I
Strawn et al, 2020	Escitalopram	2.56	1.20	5.49	16 / 26	6 / 25				-	
Walkup et al, 2008	Sertraline	2.32	1.50	3.57	73 / 133	18 / 76			-	-	
		2.11	1.50	2.98	124 / 212	42 / 158			•		
							0.01	0.1	1	10	100
								Favors placebo	Favo	ors pharmacoth	erapy

Abbreviations: CI=confidence interval; vs.=versus.

Appendix G Figure 22. Anxiety CBT Intervention vs. Treatment as Usual or Attention Control: Functioning (Children's Anxiety Impact Scale)

udy name	Comparison	Statistic	s for each st	udy		Sample size		Differe	ence in means and	9
		Difference in means	Lower limit	Upper limit	CBT	Waitlist/TAU/placebo				
Thirlwall et al, 2013	Combined	-5.38	-10.35	-0.41	40	48		+	—	
Waite et al, 2019	Individual child+parent internet CBT	3.97	-5.78	13.72	30	30			_	
Walkup at al, 2008	Individual in-person child-focused CBT	-1.70	-4.57	1.17	139	76		-	╼╂	
		-2.23	-5.88	1.43	209	154		-		
							-16.00	-8.00	0.00	
								Favours A		

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; TAU=treatment as usual; vs.=versus.

Appendix G Figure 23. Anxiety CBT Interventions vs. Treatment as Usual or Attention Control: Functioning (Children's Global Assessment Scale)

Study name	Comparison	Statistic	s for each st	udy		Difference	e in means a	nd 95% CI	
		Difference in means	Lower limit	Upper limit					
Cornacchio et al, 2019	Group child+parent in-person CBT	1.10	-2.37	4.57	1		-	1	- 1
Oonovan et al, 2014	Individual parent-focused internet CBT	5.06	-0.66	10.78			⊢∎	-	
lolmes et al, 2014	Group child-focused in-person CBT	12.77	6.62	18.92			-		
Sinsburg et al, 2020	Individual in-person child-focused CBT	1.76	-2.51	6.03			-		
errin et al, 2019	Individual child+parent in-person+internet CBT	22.70	17.82	27.58				-	⊢
illabo et al, 2018	Combined	9.62	6.53	12.70			- -		
laite et al, 2019	Individual child+parent internet CBT	4.30	-2.65	11.25			╅	<u> </u>	
/alkup at al, 2008	Individual in-person child-focused CBT	3.70	0.78	6.62			 -		
		7.54	2.84	12.23			■		
					-32.00	-16.00	0.00	16.00	32.0
					Fav	ors waitlist/TAU/plac	beo	Favors CBT	

Abbreviations: CBT=cognitive behavioral therapy; CI=confidence interval; TAU=treatment as usual; vs.=versus.

Appendix G Figure 24. Anxiety Pharmacotherapy Intervention vs. Placebo: Functioning (Children's Global Assessment Scale)

Study name	Comparison	Statistic	cs for each stu	ıdy	Sample siz	<u>te</u>		Difference	in means ar	nd 95% CI	
		Difference in means	Lower limit	Upper limit	Pharmacotherapy	Placebo					
Birmaher et al, 2003	Fluoxetine	9.10	3.13	15.07	37	37	1	1	1 —		- 1
Walkup et al, 2008	Sertraline	4.90	1.86	7.94	133	76					
Strawn et al, 2015	Duloxetine	4.50	1.73	7.27	135	133					
		5.14	3.21	7.08	305	246			◆		
							-32.00	-16.00	0.00	16.00	32.00
								Favors placebo	Fave	ors pharmacothe	erapy

Abbreviation: CI=confidence interval; vs.=versus.

Appendix G Figure 25. Depression Psychotherapy Interventions vs. Attention Control, Treatment as Usual, or Wait-List: Depression Symptoms (Beck Depression Inventory [BDI] or BDI II)

Study name	Comparison	Outcome	Statisti	cs for each s	tudy		Std diff	in means a	nd 95% CI	
			Std diff in means	Lower limit	Upper limit					
Clarke et al., 1999	Combined	BDI	-0.42	-0.93	0.09					
opooco et al., 2018	Internet based individual CBT	BDI-II	-0.70	-1.19	-0.22					
opooco et al., 2019	Internet based individual CBT	BDI-II	-0.81	-1.30	-0.32					
/lufson et al., 2004	Interpersonal psychotherapy	BDI	-0.37	-0.87	0.13					
			-0.58	-0.83	-0.34		l	ŧ۱		
						-16.00	-8.00	0.00	8.00	16.00
							ors psychother		Favors contro	

Abbreviations: BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CI=confidence interval; vs.=versus.

Appendix G Figure 26. Depression Psychotherapy Interventions vs. Treatment as Usual or Wait-List: Depression Symptoms (Hamilton Depression Rating Scale)

tudy name	Comparison	Statisti	cs for each stu	dy		Differenc	e in means a	and 95% CI	
		Difference in means	Lower limit	Upper limit					
larke et al., 2005	Individual in-person youth CBT	-1.60	-4.25	1.05		- 1 -		1	
larke et al., 1999	Combined	-2.05	-5.32	1.22		-	╼┼		
ufson et al., 2004	Interpersonal psychotherapy	-4.10	-8.16	-0.04		⊢	-		
		-2.25	-4.09	-0.42		l	◆		
					-16.00	-8.00	0.00	8.00	16.00
					Fav	ors psychother	apv	Favors contro	I

Appendix G Figure 27. Depression Psychotherapy Interventions vs. Treatment as Usual, Placebo, or Wait-List: Depression Symptoms (Children's Depression Rating Scale-Revised)

Study name	Comparison	Statistics	for each s	tudy	Sample si	ze		Differenc	e in means a	nd 95% CI	
		Difference in means	Lower limit	Upper limit	Psychotherapy	Control					
Clarke et al., 2016	Individual in-person youth CBT	1.90	-1.04	4.84	106	106		- 1	+-	-	
Narch et al., 2004	Individual in-person CBT	0.29	-1.97	2.55	111	112				-	
ristad et al., 2019	Family CBT	-1.00	-7.57	5.57	18	18		_		-	
		0.76	-0.97	2.48	235	236			*	-	
							-8.00	-4.00	0.00	4.00	8.00
							En	vors psychother	any Favo	rs waitlist or pla	oobo

 $\textbf{Abbreviations:} \ CBT = cognitive \ behavioral \ the rapy; \ CI = confidence \ interval; \ vs. = versus.$

Appendix G Figure 28. Depression Pharmacotherapy Interventions vs. Placebo: Depression Symptoms (Children's Depression Rating Scale-Revised)

Study name		Statistic	cs for each stu	ıdy	Sample siz	<u>te</u>		Differenc	e in means	and 95% CI	
		Difference in means	Lower limit	Upper limit	Pharmacotherapy	Placebo					
March et al., 2004	Fluoxetine	-5.47	-7.60	-3.34	109	112		-	-		
Emslie, 2009	Escitalopram	-3.30	-6.11	-0.49	129	132		-			
Vagner, 2006	Escitalopram	-1.70	-4.98	1.58	154	157		-			
		-3.76	-5.95	-1.57	392	401		◀	▶		
							-16.00	-8.00	0.00	8.00	16.00
							Favo	ors pharmacothe	erapy	Favors control	

Abbreviation: CI=confidence interval; vs.=versus.

Appendix G Figure 29. Depression Psychotherapy Interventions vs. Attention Control, Wait-List, or Placebo: Loss of Diagnosis

Study name	Comparison	Time point	Statist	ics for eac	h study	Events / To	otal		Risk ra	atio and 95	<u>% CI</u>	
			Risk ratio	Lower limit	Upper limit	Psychotherapy	Control					
Clarke et al, 1999	CBT	8 weeks	1.38	0.90	2.12	46 / 69	13 / 27		I	 	- 1	1
ΓADS (Kennard 2006)	CBT	12 weeks	1.01	0.80	1.28	53 / 87	54 / 89					
Γοροοco et al, 2018	CBT	8 weeks	4.46	2.07	9.63	24 / 33	6/37			I -	■	
Topooco et al, 2019	CBT	8 weeks	2.07	1.01	4.24	15 / 27	7 / 26			-	-	
			1.73	1.00	3.00	138 / 216	80 / 179				l	
								0.01	0.1	1	10	100
									Favor control		Favors CBT	

Appendix G Figure 30. Depression Pharmacotherapy Interventions vs. Placebo: Remission (Children's Depression Rating Scale-Revised ≤28)

Study name		Time point				Events / T	otal		Risk r	atio and 95%	<u>6 CI</u>	
			Risk ratio	Lower limit	Upper limit	Psychotherapy	Control					
Emslie et al, 2009 Es	scitalopram	8 weeks	1.17	0.88	1.54	64 / 154	56 / 157					
Wagner et al, 2006 Es	scitalopram	8 weeks	1.21	0.90	1.61	59 / 129	50 / 132					
TADS (Kennard 2006) FI	luoxetine	12 weeks	1.35	0.79	2.31	25 / 109	19 / 112			╂═╾		
			1.20	1.00	1.45	148 / 392	125 / 401			•	l	
								0.01	0.1	1	10	100
									Favor control	Favo	rs pharmacothe	erapy

Abbreviation: CI=confidence interval; vs.=versus.

Appendix G Figure 31. Depression Psychotherapy Interventions vs. Wait-List or Placebo: Functioning (Children's Global Assessment Scale)

Study name	Comparison	Statistics	s for each s	tudy	Sample siz	<u>e</u>		Differenc	e in means ar	nd 95% CI	
		Difference in means	Lower limit	Upper limit	Pharmacotherapy	Placebo					
Clarke et al., 2005	Individual in-person youth CBT	3.00	-0.16	6.16	53	50	1	1	-	-	- 1
Clarke et al., 2016	Individual in-person youth CBT	-1.77	-4.57	1.03	106	106		+	-		
March et al., 2004	Individual in-person CBT	0.70	-2.48	3.88	111	112		-		—	
Mufson et al., 2004	Interpersonal psychotherapy	7.20	0.64	13.76	34	29			—	_	>
		1.52	-1.54	4.58	304	297					
							-8.00	-4.00	0.00	4.00	8.00

Appendix G Figure 32. Depression Pharmacotherapy Interventions vs. Placebo: Functioning (Children's Global Assessment Scale)

Study name		Statistic	s for each st	udy	Sample siz	<u>te</u>		Differenc	e in means a	nd 95% CI	
		Difference in means	Lower limit	Upper limit	Pharmacotherapy	Placebo					
March et al., 2004	Fluoxetine	2.70	-0.56	5.96	109	112			┼■	— I	1
Emslie, 2009	Escitalopram	2.20	-0.93	5.33	154	157			┼╋	-	
Wagner, 2006	Escitalopram	2.90	-0.17	5.97	129	132			⊢ ∎	⊢	
		2.60	0.78	4.42	392	401				•	
							-16.00	-8.00	0.00	8.00	16.00
							Fave	ors pharmacothe	arany	Favors placebo	

Abbreviation: CI=confidence interval; vs.=versus.

Appendix G Figure 33. Anxiety CBT Interventions vs. Wait-List or Placebo: Withdrawal Due to Adverse Events

Study name	Comparison	Statis	tics for eac	h study	Ever	nts / Total		Risk r	atio and 95	% CI	
		Risk ratio	Lower limit	Upper limit	СВТ	Waitlist or placebo					
Perrin et al, 2019	Individual child+parent in-person+internet+CBT	3.00	0.13	69.52	1 / 20	0/20		1	\dashv	┷	— I
Stjerneklar et al, 2019	Individual internet child-focused CBT	0.38	0.02	9.05	0 / 34	1/39	-	_	\vdash	—	
Vaite et al, 2019	Individual child+parent internet CBT	0.13	0.01	2.53	0 / 27	2/17	⊬		+		
Valkup et al, 2008	Individual in-person CBT	0.18	0.01	4.45	0 / 139	1 / 76	⊬	- -	+	-	
		0.39	0.08	1.87	1 / 220	4 / 152					
							0.01	0.1	1	10	100
								Favors CBT	Fav	ors waitlist/plac	cebo

Appendix G Figure 34. Anxiety Pharmacotherapy Interventions vs. Placebo: Withdrawal Due to Adverse Events

Study name		Statis	ics for eac	ch study	Events / To	<u>tal</u>		Risk	ratio and 9	<u>5% C</u> I	
		Risk ratio	Lower limit	Upper limit	Pharmacotherapy	Placebo					
Birmaher et al, 2003	Fluoxetine	13.00	0.76	222.75	6 / 37	0 / 37	- 1		+-	- = -	\longrightarrow
Pine et al, 2001	Fluvoxamine	5.16	0.62	42.93	5 / 63	1 / 65			+	-	-
Strawn et al, 2015	Duloxetine	1.18	0.41	3.43	7 / 135	6 / 137				-	
Strawn et al, 2020	Escitalopram	0.96	0.06	14.55	1 / 26	1 / 25		+	-+-		
Walkup et al, 2008	Sertraline	0.19	0.01	4.64	0 / 133	1 / 76	←			-	
		1.72	0.57	5.18	19 / 394	9 / 340			-	▶	
							0.01	0.1	1	10	10

Abbreviation: CI=confidence interval; vs.=versus.

Overview

Appendix H includes a synthesis of results for symptoms other than those directly targeted by the intervention, specifically, anxiety and depression for suicide risk interventions; depression for anxiety interventions; and anxiety for depression interventions.

Suicide Risk

Results: Anxiety Symptoms

Psychotherapy vs. Treatment as Usual or Attention Control

Three studies reported on the effects of suicide or self-harm interventions on anxiety symptoms at the end of treatment (1 month to 12 weeks). ^{94, 100, 144} Studies compared MBT, ⁹⁴ IPT-A-IN, ¹⁴⁴ child interview with counseling, ¹⁰⁰ parent sessions, ¹⁰⁰ or child interview with counseling plus parent sessions ¹⁰⁰ with TAU. Two of the interventions ^{94, 144} were high contact (>3 sessions), and one intervention ¹⁰⁰ was low contact (<3 sessions). The results could not be pooled because of differences in measures; the findings were mixed. Reported anxiety measures included the RCADS, ⁹⁴ BAI, ¹⁴⁴ and four individual anxiety items (e.g., "I feel uneasy or anxious"). ¹⁰⁰ Study sample sizes ranged from 53 to 615. Statistically significant improvement in anxiety symptoms was reported for the treatment arms of the IPT-A-IN (11.94 vs. 25.45, p<0.001), ¹⁴⁴ child interview with counseling (rate of change: -0.683 vs. -0.440, p<0.05), and child interview with counseling plus parent sessions (rate of change at 1 month: -0.849 vs. -0.440, p<0.001)¹⁰⁰ at the end of treatment. No significant differences were reported on the RCADS at the end of treatment between MBT and TAU. ⁹⁴ One study of child interview with counseling plus parent sessions continued to report statistically significant differences between arms at 1 month in addition to 2.5 months and continued to find statistically significant differences between arms. ¹⁰⁰

Results: Depression Symptoms

Psychotherapy vs. Treatment as Usual or Attention Control

Thirteen studies reported on the effects of suicide or self-harm interventions on depression symptoms at the end of treatment (2 weeks to 12 months). ^{80, 82, 93-95, 97, 100, 107, 108, 115, 128, 144, 159, 199-203} Included studies compared family therapy, ^{80, 199, 200} attachment-based therapy, ⁸² group psychotherapy, ^{93, 95} MBT, ⁹⁴ internet-based CBT, ⁹⁷ child interview with counseling, ¹⁰⁰ parent sessions, ¹⁰⁰ child interview with counseling plus parent sessions, ¹⁰⁰ youth-nominated support team, ¹⁰⁸ motivational interviewing, ¹⁰⁷ DBT, ^{115, 201-203} mentalization-based treatment, ¹²⁸ IPT-A-IN, ¹⁴⁴ and developmental group therapy. ¹⁵⁹ Overall nine trials ^{80, 82, 93-95, 115, 128, 144, 159, 199-203} examined high-contact interventions (>3 sessions), and four trials ^{97, 100, 107, 108} examined limited-contact interventions (<3 sessions). Twelve studies compared intervention with TAU, ^{80, 82, 93-95, 100, 107, 108, 115, 128, 144, 159, 199-203} and one study compared intervention with attention control. ⁹⁷ Studies reported on a variety of instruments including the BDI-II, CDRS-R, CES-D, MADRS, MFQ, RCADS, RCADS-2-SF, and SMFQ. Study sample sizes ranged from 49 to 832. The most commonly reported measure was the MFQ.

Appendix H. Results of Treatment for Off-Target Conditions and Symptoms

Five studies reported on the MFQ^{93, 95, 128, 159} or SMFQ at the end of treatment. The MFQ is a 13-item self-report measure with a range of 0 to 68. A cutoff of 28/29 discriminates between adolescents with major depression and those with subthreshold depression or with no depressive disorder. Posttreatment MFQ scores in the intervention arms ranged from 21.9 to 30.91, while scores in the control arm ranged from 23.4 to 32.38. The SMFQ is a 13-item self-report measure with a range of 0 to 26. A general cutoff of 8 discriminates between children and adolescents with clinical depression. For one study that reported an SMFQ score, the posttreatment mean score in the intervention arm was 10.2, while the mean score in the control arm was 12.6. Of these five studies, the standardized mean difference was -0.17 (**Appendix H Figure 1**, 95% CI, -0.43 to 0.09; N=633, *I*²=52%). One study of group psychotherapy continued to find no statistically significant differences between group psychotherapy and routine care at 12 months.⁹³ A study of group therapy continued to find no statistically significant differences between group therapy and routine care at 12 months.⁹⁵

Seven studies reported on other depression measures (BDI-II, CDRS-R, RCADS, RCADS-2-SF, and MFQ) at the end of treatment (2 weeks to 12 months). ^{80, 82, 94, 97, 107, 108, 128, 144, 199, 200, 221} Three studies reported statistically significant differences between groups; one on the BDI-II (19.97 vs. 31.58, p<0.001), ¹⁴⁴ one on the MFQ (9.26 vs. 11.54, p<0.05), ¹²⁸ and one on RADS-2-SF (25.38 vs. 30.87, p<0.01) favoring intervention. ¹⁰⁷ One study ¹⁰⁰ reported that child interview with counseling and the combination of child interview with counseling plus parent sessions significantly improved CES-D scores compared with TAU (rate of change: -0.951 vs. -0.685, p<0.01; rate of change: -1.021 vs. -0.685, p<0.01). Within the same study, parent-only sessions did not significantly improve depression scores. Six studies reported no statistically significant differences between intervention and TAU; of these, two reported on the CDRS-R; ^{80, 108, 199, 200} one each reported on the BDI-II, ⁸² RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸² MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸⁰ MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸⁰ MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80, 199, 200} BDI-II, ⁸⁰ MFQ, ⁹³ RCADS-MD, ⁹⁴ and RADS-2. ⁹⁷ Five studies reported on the CDRS-R, ^{80,}

One study reported on remission of depression symptoms based on the BDI-II.⁸² Remission was defined as a BDI-II score \leq 9. The study reported no statistically significant differences between attachment-based therapy and enhanced usual care at the end of treatment (12 weeks, OR 2.70; 95% CI, 1.03 to 17.07; p=0.06) or at 24 weeks (OR, 2.21; 95% CI, 0.76 to 6.42; p=0.14).

Anxiety

Results: Depression Symptoms

Psychotherapy vs. Wait-List Controls, Treatment as Usual, or Placebo

In addition to reporting on anxiety symptom outcomes, 10 studies reported on depression symptoms. ^{65, 70, 103, 112, 120, 122, 141, 145, 152, 153, 205-211} Four studies reported CDI outcomes at the end of treatment (data were reported at 8 to 16 weeks from baseline). ^{70, 103, 112, 120} CDI total scores ranged from 0 to 54 with a cutoff of 17 to 19 indicating a clinically relevant level of depressive symptoms. ²²² Three studies had two active arms compared with the wait-list condition: telephone vs. email vs. client initiated "on their own," ¹¹² child focused vs. child and parent focused ^{120, 212} or child plus family focused. ⁷⁰ Posttreatment scores in the CBT arms ranged from 4.1 to 14.6, while

Appendix H. Results of Treatment for Off-Target Conditions and Symptoms

scores in the wait-list arm ranged from 6.8 to 19.1. The pooled mean difference, averaging across multiple study arms in studies with more than one active arm, was -2.80 (**Appendix H Figure 2**, 95% CI, -4.74 to -0.86; N=280; k=4; I^2 =0%).

Four studies reported child-rated short-MFQ scores at the end of treatment (data were reported at 10 to 17 weeks from baseline). ^{65, 141, 145, 152} Child-rated short-MFQ scores ranged from 0 to 26²²³ with a cutoff of 10 to 12 commonly used to indicate the presence of depression. One study had two active arms compared with a wait-list condition: brief vs. full CBT. ¹⁴⁵ Posttreatment scores in the CBT arms ranged from 3.0 to 8.1, while scores in the wait-list arm ranged from 5.2 to 7.8. The pooled mean difference, averaging across multiple study arms with more than one active arm, ¹⁴⁵ was -1.14 (**Appendix H Figure 3,** 95% CI, -2.35 to 0.06; N=379; k=4; *I*²=4%).

The same four studies also reported on parent-rated short-MFQ measures, but the respondent (mother vs. father) varied by study. $^{65, 141, 145, 152}$ Two studies reported separately on ratings from mothers and fathers, $^{65, 141}$ and two reported a single rating for parents. $^{145, 152}$ Posttreatment scores in the CBT arm ranged from 2.0 to 7.2, while scores in the wait-list arm ranged from 4.9 to 9.5. The pooled mean difference, averaging across multiple study arms with more than one active arm and across parental measures, was -1.89 (**Appendix H Figure 4**, 95% CI, -3.04 to -0.74; N=367; k=4; I^2 =0%).

Two studies reported child-rated MFQ outcomes at the end of treatment (data were reported at 10 to 12 weeks from baseline). 122, 153, 205-211 Child-rated MFQ²²⁴ scores ranged from 0 to 66 with a cutoff score of 27 to 29 commonly used to indicate the presence of depression. Posttreatment scores ranged from 4.6 to 6.9 in the CBT arms, while scores in the wait-list arms ranged from 6.4 to 25.4. One study¹²² reported a statistically significant difference between arms favoring CBT (effect size partial eta squared=0.40, p<0.001). The other study did not find a statistically significant difference. 153, 205-211, 216 The same two studies reported parent-rated MFQ outcomes at the end of treatment. 122, 153, 205-211 Posttreatment scores ranged from 4.1 to 10.1 in the CBT arm, while scores in the wait-list arm ranged from 8.0 to 20.9. One study reported statistically significant differences between arms favoring CBT (effect size partial eta squared=0.19, p<0.01). 122 The second study did not report a statistically significant difference. 153, 205-211

One study reported DSRS outcomes at the end of treatment (data were reported at 8 or 16 weeks from baseline). One Study reported DSRS scores ranged from 0 to 36 with a cutoff score of 16 used to indicate depression. No statistical difference was found on the DSRS.

Pharmacotherapy vs. Placebo

In addition to reporting on anxiety symptom outcomes, two sertraline studies (N=22 and N=209) reported on three different measures of depression symptoms at the end of treatment: clinician-rated HAM-D, parent-rated MFQ, and child-rated MFQ. 130, 153, 205-211, 216 The results were consistent for HAM-D and parent-rated MFQ in reporting statistically significant benefits for sertraline. One study found a statistically significant difference in HAM-D scores at 9 weeks from baseline when compared with placebo (4.0 vs. 11.5, p<0.001). A HAM-D score of less than 8 is generally 226 considered to be within the normal range. The second study found a statistically significant difference in parent-rated MFQ scores at 12 weeks from baseline when compared with placebo (5.0 vs. 8.0, p<0.001) but no differences in child-rated MFQ scores. An

Appendix H. Results of Treatment for Off-Target Conditions and Symptoms

MFQ score of 12 or higher may indicate depression.²⁰⁵ Both arms reported MFQ scores of 13 or higher in both arms at baseline and scores below 12 at followup.²⁰⁵

Combination Therapy (Sertraline Plus CBT) vs. Placebo

One study reported on outcomes comparing sertraline plus CBT with placebo. $^{153, 205-211, 216}$ The study reported parent and youth-reported MFQ scores. Results varied by respondent. Parent-reported measures at followup favored combination therapy $(4.1\pm7.2 \text{ vs. } 8.0\pm7.5, \text{ adjusted p}<0.001)$; youth measures were not statistically significantly different.

Depression

Results: Anxiety Symptoms

Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo

Two studies of internet-delivered CBT compared with placebo reported two measures of anxiety symptoms, the BAI and SIAS. Neither found a statistically significant difference between internet-delivered CBT and placebo at 8 weeks.^{147, 148}

Pharmacotherapy vs. Placebo

None of the included studies reported anxiety outcomes.

Combination Therapy (Fluoxetine Plus CBT) vs. Placebo

The study did not report anxiety outcomes.

Collaborative Care vs. Treatment as Usual

The study did not report anxiety outcomes.

Appendix H Figure 1. Depression Symptoms for Suicide and Self-Harm Interventions: Pooled Estimates of Effect

Suicide Treatment on MFQ or SMFQ Study name Time point Statistics for each study Sample size Std diff in means and 95% CI Std diff Upper p-Value Treatment Control Green, 2011 6 months -0.030 -0.240 0.180 0.777 171 178 0.599 Hazell, 2009 -0.125 -0.591 0.341 34 37 8 weeks Melhlum, 2014 -0.309 -0.759 0.140 0.177 39 38 Rossouw, 2012 12 months -0.646 -1.096 -0.196 0.005 40 40 0.239 0.373 Wood, 2001 7 months -0.287 0.765 29 27 -0.168 -0.427 0.091 0.204 -2.00 1.00 2.00

Favors Treatment

Favors Control

I-squared: 52.53; p=0.08

Abbreviations: CI=confidence interval; MFQ=Mood and Feelings Questionnaire; SMFQ=Short Mood and Feelings Questionnaire.

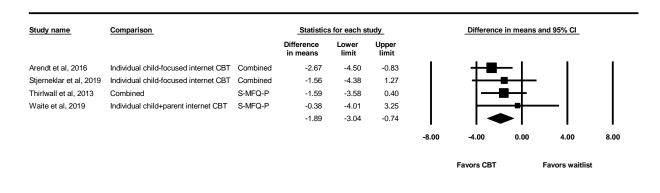
Appendix H Figure 2. Children's Depression Inventory Scores for CBT for Anxiety in Children and Adolescents

Study name	Comparison	Stat	istics for e	ach study	<u></u>		Difference	in means ar	nd 95% CI	
		Difference in means	Lower limit	Upper limit	p-Value					
Barrett et al, 1996	Combined	-2.500	-5.185	0.185	0.068		+=	\dashv		
Ishikawa et al, 2019	Individual child+parent in-person CBT	-4.410	-9.411	0.591	0.084	₭—	-	+		
Lyneham et al, 2006	Combined	-2.047	-6.640	2.547	0.383	-	- =	+	-	
Ost et al, 2015	Combined	-3.150	-8.169	1.869	0.219	(- = -	+		
		-2.804	-4.743	-0.864	0.005			-		
						-8.00	-4.00	0.00	4.00	8.00
							Favors CBT	ı	Favors waitlist	

Appendix H Figure 3. Short Mood and Feelings Questionnaire-Child for CBT for Anxiety in Children and Adolescents

Study name	Comparison	Statistics for each study				Difference in means and 95%				
		Difference in means	Lower limit	Upper limit						
rendt et al, 2016	Group child+parent in-person CBT	-2.23	-3.96	-0.50		⊢∎	⊢ l	1		
Stjerneklar et al, 2019	Individual child-focused internet CBT	0.29	-3.40	3.98		I—	-			
Thirlwall et al, 2013	Combined	-0.09	-2.13	1.96		-	_#	.		
Vaite et al, 2019	Individual child+parent internet CBT	-1.22	-4.63	2.19		+		-		
		-1.14	-2.35	0.06		-				
					-8.00	-4.00	0.00	4.00	8.00	
						Favors CBT		Favors waitlis		

Appendix H Figure 4. Short Mood and Feelings Questionnaire-Parent, Mother, or Father for CBT for Anxiety in Children and Adolescents



Appendix H Table 1. Psychotherapy vs. Wait-List Controls, Treatment as Usual, Attention Control, or Placebo for Depression in Children: Anxiety Symptom Improvement Scales

					Time		Treatment		Placebo	Between-	Between-
Treatment		Mean Age	Intervention and	Outcome	Point	Treatment		Placebo	Mean	Group	Group P-
(Condition)	Author, Year	(SD)	Duration	Measure	(Weeks)		Score (SD)		Score (SD)	Difference	Value
Internet-	Topooco et al,	IG1: 17.2	Internet-based CBT	BAI	8 weeks	33	20.6 (9.0)	37	19.4 (8.6)	1.20	N=NS
based	2018 ¹⁴⁷	(1.0)	with 8 skill-based								
individual		CG: 16.9	modules plus weekly								
CBT vs.		(1.1)	30-minute chat								
attention			sessions with therapist								
control			over 8 weeks								
	Topooco et al,	IG1: 17.2	Internet-based CBT	SIAS	8 weeks	33	39.3 (13.8)	37	41.4 (11.8)	-2.10	N=NS
	2018147	(1.0)	with 8 skill-based								
		CG: 16.9	modules plus weekly								
		(1.1)	30-minute chat								
			sessions with therapist								
			over 8 weeks								
	Topooco et al,	IG1: 17.5		BAI	8 weeks	35	16.6 (10.3)	35	20.0 (9.3)	-3.40	p=NS
	2019 ¹⁴⁸	(1.1)	with 8 skill-based								
		CG: 17.5	modules plus weekly								
		(1.2)	45-minute chat								
			sessions with therapist								
			over 8 weeks								
	Topooco et al,	IG1: 17.5		SIAS	8 weeks	35	35.4 (19.0)	35	35.1 (14.3)	0.30	p=NS
	2019 ¹⁴⁸	(1.1)	with 8 skill-based								
			modules plus weekly								
		(1.2)	45-minute chat								
			sessions with therapist								
			over 8 weeks								

Abbreviations: BAI=Beck Anxiety Inventory; CBT=cognitive behavioral therapy; CG=control group; IG=intervention group; N=number; NS=not significant; SD=standard error; SIAS=Social Interaction Anxiety Scale; vs.=versus.

Appendix I Table 1. Anxiety Diagnostic Test Accuracy Studies: Study Characteristics (KQ 2)

Author, Year Quality	Country Funding	Recruitment and Setting	Age Range, Years	Total N Sex (% Female)	Index Test(s)	Reference Measure	Time Between Index Test and Reference Measure
Bailey et al, 2006 ²¹ Fair	U.S. NIMH	Random sample of families from a southern California university-affiliated pediatric primary care service	8 to 17	190 (49)	SAS-C/P SAS-A/P SCARED-P SP SWQ-P	ADIS-C/P	NR
Canals et al, 2012 ¹⁶² Fair	Spain Spanish Ministry of Health and Consumption	Recruited from 7 state and 6 state-subsidized private schools in one medium sized city in Catalonia, Spain	9 to 13	562 (55)	SCARED-C SCARED-C Short SCARED-P SCARED-P Short	MINI Kid	Within a week
Garcia-Lopez et al, 2015 ¹⁶⁴ NR Fair	Spain Spanish Ministry of Higher Education and the European Regional Development Fund	Recruited from public and private schools in a medium-size state in the south of Spain	12 to 18	1,034 (54)	EDAS* LSAS-CA* SAS-A* SASA SoPhI* SPAI-B SPIN* Mini SPIN*	ADIS-C/P	NR
Johnson et al, 2002 ¹³ Fair	Aaron Diamond	Primary care and school nurses' offices in California, Ohio, New Jersey, and New York; rural, urban, and suburban sites	13 to 18	403 (63)	PHQ-A	Clinical interview	NR
Muris et al, 2001 ¹⁶⁹ Fair	The Netherlands NR	Recruited from 10 primary schools in one region; 5 each from urban and rural communities	7 to 14	82 (61)	SCARED	KSCID	NR
O'Connor et al, 2016 ¹⁴ Fair	U.K. GL Assessment	Recruited from 8 hospital pediatric outpatient departments. Clinical samples from a child and adolescent mental health service and hospital-based pediatric psychology service, all in Scotland	8 to 17	100 (48†)	PI-ED	C-DISC	Same time

Appendix I Table 1. Anxiety Diagnostic Test Accuracy Studies: Study Characteristics (KQ 2)

Author, Year Quality	Country Funding	Recruitment and Setting	Age Range, Years	Total N Sex (% Female)	Index Test(s)	Reference Measure	Time Between Index Test and Reference Measure
Fair	University of Miami, Department of	Recruited from 2 pediatric primary care clinics in a large urban area in southeastern U.S.	12 to 17	71 (43)	ANS-2 questions ANS-3 questions ANS-5 questions	ADIS-IV-C	Within 1 month
Ranta et al, 2007 ¹⁷⁰ Fair		Recruited from 2 secondary schools in Ylojarvi, Finland	12 to 17	350 (49)	SPIN	K-SADS-PL	Within 1 month
,		Recruited from 2 secondary schools in Ylojarvi, Finland	12 to 17	350 (49)	_	K-SADS-PL K-SADS (subclinical)	Within 1 month
	National Science Council, Taiwan	Recruited from 3 public junior high schools in 3 rural areas of Taiwan (randomly invited)	13 to 15	144 (50†)	SPIN	MINI-Kid	4 weeks

^{*}No accuracy data provided, so not included in summary of evidence.

Abbreviations: ADIS-IV-C=Anxiety Disorders Interview Schedule for DSM-IV for Children; ADIS-C/P=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children/Parents; ANS=Autonomic Nervous System Questionnaire; C-DISC=computerized diagnostic schedule for children; EDAS=escala para la deteccion de ansiedad socia; KQ=key question; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children; K-SADS-PL=Schedule for Affective Disorders and Schizophrenia for School-Age Children-present and lifetime version; KSCID-child edition of the structured clinical interview for DSM-IV; LSAS-CA=Social Anxiety Scale for Children and Adolescents; MINI-Kid=MINI international neuropsychiatric interview for kids; N=number; NUMH=National Institute of Mental Health; NR=not reported; PHQ-A=Patient Health Questionnaire-Adolescent; PI-ED=Pediatric Index of Emotional Distress; SAS-A/SASA=social anxiety scale-adolescents; SAS-A/P=social anxiety scale-adolescents; SAS-C/P=social anxiety scale children/parents; SCARED-Screen for Anxiety Related Emotional Disorders for Children; SCARED-P=Screen for Anxiety Related Emotional Disorders-Parents; SP=social phobia; SoPhI=social phobia inventory; SPAI-B=Brief form of the Social Phobia and Anxiety Inventory; SPIN=Social Phobia Inventory; SWQ-P=social worries questionnaire-parents; U.K.=United Kingdom; U.S.=United States.

[†]Percentage of those in Phase 1.

Appendix I Table 2. Suicide Risk Harms of Screening Studies: Study Characteristics (KQ 3)

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Gould et al, 2005 ⁶³ None	U.S. Cluster-RCT NIMH	high schools in New	Mental health screening that included questions on suicidal ideation and behaviors on two surveys administered 2 days apart.	Mental health screening that did not include questions on suicidal ideation and behaviors on the first of two surveys administered 2 days apart.	
Robinson et al, 2011 ⁶⁴ None	Australia Cross-over RCT Bennelong Foundation; Lord Mayor Foundation, Rotary Club of Camberwell, Australian Rotary Health Research Fund	entry government school in Melbourne	intervention group received the embedded tool on Day 1.	embedded in an online questionnaire used to	Fair

Abbreviations: KQ=key question; RCT=randomized, controlled trial; NIMH=National Institute of Mental Health; U.S.=United States.

Appendix I Table 3. Suicide Risk Harms of Screening Studies: Population Characteristics (KQ 3)

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
			Students/parents "opting out" of	NR
	, ,	in a participating high school	participation	
	Race/ethnicity: 80.3% White,			
	5.1% Black, 7.3% Hispanic, 3.8%			
	Asian, and 3.5% other			
Robinson et al, 2011 ⁶⁴	Age: NR (all were Year 10	Year 10 student at Melbourne	Did not consent to participate	NR
None	students)	High		
	Female: 0 (0)			
	Race/ethnicity: NR			
	,			

Abbreviations: KQ=key question; N=number; NR=not reported; SD=standard deviation.

Appendix I Table 4. Suicide Risk Harms of Screening Studies: Outcomes (KQ 3)

Author, Year Registry Number	Harm Outcomes
Gould et al, 2005 ⁶³	Distress as measured by POMS-A subscale, mean (SD)
None	At baseline
	Intervention: 6.9 (10.0)
	Control: 6.4 (9.7); P=0.25
	Immediately after first survey
	Intervention: 5.5 (9.7)
	Control: 5.1 (10.0); P=0.66 Before second survey 2 days later
	Intervention: 4.3 (9.0)
	Control: 3.9 (9.4); P=0.41
	Suicidal ideation as measured by SIQ-Jr, mean (SD)
	On second survey 2 days later
	Intervention: 6.5 (11.5)
	Control: 6.6 (10.5), P=0.86
	Interim suicidality thoughts between 1st and 2nd surveys, %
	Intervention: 4.7%
	Control: 3.9%; OR, 1.20 (95% CI, 0.72 to 2.00)
Robinson et al, 2011 ⁶⁴	Distress as measured by POMS-A
None	Day 1 questionnaire
	No significant difference between groups on 5 subscales (Anger, Confusion, Depression, Fatigue, Tension); significant difference on the vigor subscale (P=0.0001)
	Change between Day 1 and Day 2 questionnaire
	No significant difference between groups on 5 subscales (Anger, Confusion, Depression, Fatigue, Tension); significant difference on the vigor subscale (P=0.000)
	Distress as measured by the item "How distressing did you find answering questions about self-harm and suicidal ideation?," N (%)
	Overall (not reported by group):
	Not at all distressing: 135 (50)
	A little distressing: 85 (31.5)
	Moderately distressing: 14 (5.2) Very distressing: 10 (3.7)
	Not sure: 26 (9.6)
Abbreviations: CI-confide	ence interval: KO=key question: N=number: OR=odds ratio: POMS-A=Profile of Mood States in Adolescents: SD=standard deviation: SIO-Jr=Suicidal

Abbreviations: CI=confidence interval; KQ=key question; N=number; OR=odds ratio; POMS-A=Profile of Mood States in Adolescents; SD=standard deviation; SIQ-Jr=Suicidal Ideation Questionnaire Junior.

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Asarnow et al, 2017 ⁶⁶ NCT00692302	National Institute of	ED, inpatient/partial hospitalization, and outpatient services	IG1: CBT (N=20) Description: SAFETY is a family-centered treatment. Two therapists work with each family—one focuses on the youth, the other on the parents/caregivers. Sessions began with	CG: TAU (N=22) An in-clinic parent session, followed by ≤3 telephone calls aimed at supporting motivation/actions to obtain followup treatment	Fair
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	National Institute for Health Research (NIHR) Health	Direct community referrals to CAMHS and hospital referrals following emergency attendance resulting from self-harm	IG1: Family therapy (N=415) Description: Between six and eight 75-minute family therapy sessions occurred over the course of 6 months (Self-harm Intervention Family Therapy [SHIFT]). Family therapists worked in groups of 3 with one therapist interviewing and two observing the family during each session. Sessions followed the Leeds Family Therapy &	CG: TAU (N=417) TAU involved a range of individual and family- oriented work delivered by local CAMHS teams with various theoretical orientations (e.g., supportive therapy/counseling, CBT, family work)	Good

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Diamond et al, 2010 ⁸² NCT00604097	U.S. RCT Centers for Disease Control and Prevention	room of children's hospital in Philadelphia, Pennsylvania	Started with treatment to reframe the relationship with relevant family members as the initial treatment goal. Included 1 to 2 sessions with adolescent alone, to identify family conflicts linked to suicide. Included 1 to 2 sessions with parent	CG: Enhanced Usual Care (N=31) Facilitated referral process with ongoing clinical monitoring and received weekly monitoring and access to a 24-hour crisis phone	Fair
Green et al, 2011 ⁹³ ISRCTN 20496110	Other very high HDI United Kingdom RCT Health Foundation; University of Manchester	and adolescent mental health services teams in northwest England	Description: Manual-based developmental group psychotherapy designed for self-harming adolescents based on techniques from CBT,	CG: Routine care (N=183) Standard psychotherapy care excluding any group intervention. Mean (SD) number of sessions was 9.7 (10.4)	Good

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Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Griffiths et al, 2019 ⁹⁴ NCT02771691	United Kingdom RCT Edinburgh and Lothians Health Foundation	Recruited from NHS Child and Adolescent Mental Health Services, which provides outpatient and specialist mental health services	Description: Up to 12 75-minute sessions of mentalization based therapy (MBT) delivered by trained MBT therapists under the supervision of an MBT-accredited supervisor, up to 10 participants per group. Duration: 12 weeks	CG: TAU (N=27) Treatment as usual, receiving tier 3 or tier 4 of usual CAMHS services, which could include psychosocial treatment or medication by team of multidisciplinary providers in outpatient settings (tier 3) or intensive community treatment, day programs, or an inpatient unit.	Fair
Hazell et al, 2009 ⁹⁵ ACTRN12608000532303	Other very high HDI Australia RCT NR	and adolescent mental health service in	IG1: Group therapy (N=35) Description: Initially six 1-hour weekly sessions focused on relationships, school and peer relationships, family problems, anger management, depression and self-harm, and hopelessness and feelings about the future. After completion of initial 6 sessions, adolescents could attend group sessions for up to 12 months. Continued to receive routine care from their adolescent mental health service. Routine care generally consisted of individual counseling, family sessions, medication assessment and review, and other care coordination activities. Duration: Up to 12 months	CG: Routine care (N=37) Routine care generally consisted of individual counseling, family sessions, medication assessment and review, and other care	Good
Hill et al, 2019 ⁹⁷ NR	U.S. RCT American Psychological Foundation; Florida International University Doctoral Evidence Acquisition Award		IG1: Internet CBT (N=40) Description: Two 20- to 30-minute web-based sessions drawing on interpersonal-psychological theory of suicide and CBT, called LEAP by study authors. Also received email regarding psychoeducational information about mental health, suicide risk factors, and local and national resources for mental health treatment and suicide/crisis counseling. Duration: 2 sessions 1 week apart	CG: Information-only control (N=40) Received email regarding psychoeducational information about mental health, suicide risk factors, and local and national resources for mental health treatment and suicide/crisis counseling.	Good

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Hooven et al, 2012 ¹⁰⁰	U.S. RCT NR	public high schools—14 traditional and 6 alternative in Seattle area.	l .	CG: TAU (N=143) One brief 30-minute interview including addressing suicide risk factors. Received connection to school resources and parent telephone call.	Fair

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
King et al, 2015 ¹⁰⁷ NR	U.S. RCT NR	Recruited from a hospital emergency department in a relatively underserved, low-income community	screening responses. Participated in an adapted motivational interview (approximately 35-45	CG: Enhanced TAU (N=22) Enhanced TAU included provision of a crisis card with suicide emergency phone numbers and written information about depression, suicide risk, firearm safety, and local mental health services.	Fair
King et al, 2009 ¹⁰⁸ NCT00071617	U.S. RCT NIMH	NR	Description: Adolescents were asked to nominate caring adults with whom they would like to have regular supportive contact following their hospitalization for suicidal ideation or attempt. Individual or group psychoeducation sessions	CG: TAU (N=225) TAU could have included psychotherapy sessions, psychoactive medication, medication followup, alcohol/drug treatment, psychiatric hospitalization, and/or residential treatment.	Fair

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³ NCT00675129	Norway RCT Norwegian Directorate of Health, the South Eastern Regional Health Authority, Extra Foundation for Health and Rehabilitation, University of Oslo	psychiatric outpatient clinics in Oslo	Description: DBT included 1 weekly session of individual therapy (60 minutes), 1 weekly session of multifamily skills training (120 minutes), and family therapy sessions and telephone coaching with individual therapists outside therapy sessions as needed over 19 weeks. Duration: 19 weeks	per patient throughout the trial) delivered by therapists who were not trained in or practicing DBT. Therapy was psychodynamically oriented or CBT combined with medication but was not manualized or checked for fidelity.	Good
Ougrin et al, 2013 ¹²¹ Ougrin, 2011 ²⁰⁴ ISRCTN 81605131	United Kingdom RCT Psychiatry Research Fund (Institute of Psychiatry, King's College London), Maudsley Charitable Funds (South London and	departments of four inner-London hospitals or	evaluation, standard disposition planning plus a brief 30-minute therapeutic intervention Duration: 1 session	CG: Assessment as usual (N=35) 1-hour standard psychosocial evaluation and standard disposition planning	Fair

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Pineda et al, 2013 ¹²⁵ ACTRN12613000668707		emergency departments of 2 hospitals and the community mental health service in the Blacktown–Mount Druitt Local Government Area (LGA) of Sydney, Australia	IG1: RAP-P (Family Intervention) (N=24) Description: Interactive psychoeducation program for parents of adolescents implemented over four 2-hour sessions (held once a week or once every 2 weeks). Parents were provided information to enhance their understanding of suicidal or self-injurious behavior, practical strategies to help their adolescent avoid or minimize their self-injurious behavior, and information to facilitate access to appropriate support services. Also received crisis management and safety planning. Duration: 4 to 8 weeks (4 sessions, held once a week or once every 2 weeks)	Any intervention deemed necessary by the adolescent's treatment team other than the family intervention program trialed. Family intervention limited to crisis management and safety planning. No structured intervention.	Fair
Rossouw et al, 2012 ¹²⁸ ISRCTN95266816	Other very high HDI United Kingdom RCT NR	individuals presenting with self- harm to community mental health services or acute hospital emergency	IG1: Mentalization-based treatment for adolescents (MBT-A) (N=40) Description: Weekly 50-minute individual MBT-A sessions and monthly 50-minute mentalization-based family therapy (MBT-F) with a focus on impulsivity and affect regulation. Duration: 12 months	CG: TAU (N=40) TAU treatments were delivered by fully qualified child mental health professionals, not manualized but based on U.K. National Institute for Health and Clinical Excellence guidance.	Fair
Tang et al, 2009 ¹⁴⁴	Other very high HDI Taiwan RCT NR	high school located in a city in southern Taiwan	IG1: Interpersonal psychotherapy (N=35) Description: Two 50-minute face-to-face weekly sessions of interpersonal psychotherapy and a 30-minute weekly telephone followup provided by trained school counselors Duration: 6 weeks	CG: TAU (N=38) Received school-based psychoeducation and irregular individual supportive counseling one or two times per week in the 6-week period. Supportive sessions were 30 to 60 minutes each and parents were invited to join sessions if needed.	Fair

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Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Wood et al, 2001 ¹⁵⁹	United Kingdom RCT Mental Health Foundation and the	and adolescent mental health service in South Manchester, England	IG1: Developmental Group Therapy (N=32) Description: Designed to meet the needs of adolescents and focus on the adolescent growing through difficulties by using positive corrective therapeutic relationships. Based on principles of problem-solving and CBT, DBT, and psychodynamic group therapy. Structured as 6 acute group sessions, followed by weekly long- term groups. Individual sessions usually done when extra cognitive behavioral work was needed. Participants had access to routine care that included family sessions, nonspecific counseling with the adolescent, and psychotropic medication. Duration: Median of 8 group sessions (range, 0 to 19) and 2.5 individual sessions (range, 0 to 10) over 6 months.	CG: Treatment as usual (N=31) TAU included routine care that would normally be provided including a variety of interventions including family sessions, nonspecific counseling with the adolescent, and psychotropic medication.	Good

Abbreviations: ABFT=Attachment-based Family Therapy; CAMHS=Child and Adolescent Mental Health Services; C-CARE=Counselors Care, Assess, Respond, Empower; CBT=cognitive behavioral therapy; CG=control group; DBT=dialectical behavior therapy; ED=emergency department; EUC=enhanced usual care; HDI=Human Development Index; HTA=health technology assessment; IG=intervention group; KQ=key question; LEAP=Learn, Explore, Assess you options, Plan; LGA=local government area; MBT=mentalization-based treatment; MBT-A=mentalization-based treatment for adolescents; MBT-F= mentalization-based treatment-family; N=number; NHS=National Health Service; NIHR=National Institute for Health Research; NIMH=National Institute of Mental Health; NR=not reported; P-CARE=Parents-Counselors Care, Assess, Respond, Empower; RAP-P=Resourceful Adolescent Parent Program; RCT=randomized, controlled trial; SAFETY=Safe Alternatives for Teens and Youths; SD=standard deviation; SHIFT=self-harm intervention family therapy; TAU=treatment as usual; U.K.=United Kingdom; U.S.=United States.

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Asarnow et al, 2017 ⁶⁶ NCT00692302	Mean age (SD): 14.6 (1.8) N (%) Female: 37 (88) Race/Ethnicity: White: 35 (83) Black: 2 (5) Hispanic/Latino: 9 (21) Asian: 5 (12) Other: 3 (7)	Children and adolescents ages 11 to 18 years living in stable family situation with a recent (past 3 months) SA or NSSI as primary problem, with the additional requirement of repetitive SH (≥3 lifetime SH episodes).	Symptoms interfering with participation in assessments/intervention (e.g. psychosis, substance dependence); not English speaking.	SA, past 3 months: 50% Nonsuicidal self-injury, past 3 months: 50% >1 Lifetime SA: 21% Major depression, past year: 55% Problematic substance abuse: 48%
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	Mean age (SD): 14.3 (1.4) N (%) Female: 737 (89) Race/Ethnicity: NR	Ages 11 to 17 years, self- harmed at least twice before being referred to CAMHS, and living with a primary caregiver who was willing to participate.	Serious risk of suicide, an ongoing child protection investigation in the family, pregnancy at time of trial entry, usual treatment by a specific specialist service within CAMHS, residence in a short-term foster home, moderate to severe learning disabilities, involvement in another study within the 6 months before entry to the current trial, sibling participation in the trial or treatment within CAMHS, and insufficient proficiency in English (participant or caregiver) to complete study questionnaires.	Primary/target condition % Known self-harm episodes: Two: 11% At least three: 89%
Diamond et al, 2010 ⁸² NCT00604097	Mean age (SD): 15.1 (1.5) N (%) Female: 55 (83) Race/Ethnicity: African American: 49 (74)	Ages 12 to 17 years, having suicidal thoughts, scores above 31 on the SIQ-Jr, above 20 on the BDI-II, and a parent or guardian willing to participate.	Needed psychiatric hospitalization, recently discharged from a psychiatric hospital, had current	Depressive disorder: 47% Anxiety disorder: 67% Externalizing disorder: 57%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
	Mean age (SD): 12 to 14 years, N (%) IG1: 69 (38) CG: 70 (38) 15 to 17 years, N (%) IG1: 114 (62) CG: 113 (62) N (%) Female: IG1: 171 (93) CG: 172 (94) Race/Ethnicity: Black and ethnic minority IG1: 12 (7) CG: 11 (6)	Ages 12 to 16 years with 2 or more episodes of self-harm during previous 12 months	Non-English speakers, severe low weight anorexia nervosa, current psychotic illness, attendance at special learning disability school, or current containment in secure care	Depressive disorder: 62% Behavioral disorder: 33%
	Mean age (SD): IG1: 15.4 (1.3) CG: 15.7 (1.4) N (%) Female: 38 (79) Race/Ethnicity: White Scottish: 33 (69)	months, receiving CAMHS treatment, competent, and	Severe learning disability or pervasive developmental disorder, acute psychotic episode, eating disorder in the absence of self-harm, non-English speaking, or current involvement in other ongoing treatment research	NR
	Mean age (SD): IG1: 14.6 (1.1) CG: 14.4 (1.2) N (%) Female: IG1: 32 (91) CG: 33 (89) Race/Ethnicity: NR	adolescent mental health service, and reported at least	Required more intensive treatment, could not attend groups, experiencing acute psychosis, or unlikely to benefit from group intervention (e.g., intellectual disability)	Alcohol problems: 4% Substance misuse: 0% Depression: 57% Conduct/oppositional defiant disorder: 7%

	Patient Characteristics: Age, Mean (SD)			
Author, Year, Registry	Female, N (%)			Prevalence of Psychiatric/
Number	Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Behavioral Conditions
Hill et al, 2019 ⁹⁷ NR	Mean age (SD): 16.9 (1.66) N (%) Female: 55 (69)	Ages 13 to 19 years, perceived burdensomeness score of 17 or greater on the Interpersonal Needs	Current psychosocial treatment or use of psychoactive medications (unless on a stable dose for 8 weeks or more)	NR
	Race/Ethnicity: White: 55 (68) Black: 13 (16) Asian: 6 (8) American Indian/Alaskan Native: 1 (1) Other: 7 (9)	Questionnaire Perceived Burdensomeness subscale, and having available Internet access		
Hooven et al, 2012 ¹⁰⁰	Mean age (SD): 16 (NR) N (%) Female: 369 (60) Race/Ethnicity: White: 406 (66) Mixed ethnicity: 86 (14) Asian American: 49 (8) African American: 25 (4) Latino/Hispanic: 18 (3)	Teens at risk for suicide based on Suicide Risk Screen (SRS) criteria	NR	NR
King et al, 2015 ¹⁰⁷ NR	Mean age (SD): 17.7 (1.7) N (%) Female: 39 (80) Race/Ethnicity: African American: 57 (28) Caucasian: 19 (39) American Indian/Alaska Native: 4 (2) Native Hawaiian/Pacific Islander: 2 (1) Hispanic: 2 (1) Other: 2 (1)	years with a positive suicide risk screen (C-SSRS) defined	medically unstable), significant	Recent suicidal ideation or attempt: 35% Current depressive symptoms with comorbid alcohol or drug abuse: 53%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
King et al, 2009 ¹⁰⁸	Mean age (SD): 15.6 (1.3)	Ages 13 to 17 years with	Severe cognitive impairment	Comorbid diagnoses
NCT00071617		significant suicidal ideation or	(mental retardation or acute	Depressive disorder: 88%
	N (%) Female: 319 (71)	suicide attempt within the	psychosis), direct transfer to	PTSD or acute stress disorder: 25%
		past 4 weeks, all of whom	medical unit, direct transfer to	Anxiety disorder: 29%
	Race/Ethnicity:	had been psychiatrically	residential placement, or no legal	Disruptive behavior disorder: 42%
	Caucasian: 376 (84)	hospitalized. Significant	guardian available	Alcohol or substance use disorder:
	African American: 27 (6)	ideation or attempt was		21%
	Hispanic: 9 (2)	defined by parent or youth		
	Other: 36 (8)	report on the NIMH DISC-IV.		
Mehlum et al, 2014 ¹¹⁵	Mean age (SD): 15.6 (1.5)	Ages 12 to 18 years, history	Bipolar disorder (except bipolar II),	Mean (SD) suicide attempts, lifetime:
Mehlum et al, 2016 ²⁰¹		of at least 2 episodes of self-	schizophrenia, schizoaffective	1.7 (4.2)
Mehlum et al, 2019 ²⁰²	N (%) Female: 68 (88)	harm, at least 1 within the	disorder, another psychotic	Attempted suicide last 4 months: 26%
Haga et al, 2018 ²⁰³		last 16 weeks; at least 2	disorder, intellectual disability, or	MDD: 22%
NCT00675129	Race/Ethnicity:	criteria of DSM-IV BPD (plus	Asperger syndrome	Other depressive disorder: 38%
	Norwegian: 62 (85)	the self-destructive criterion),		Panic disorder: 9%
		or, at least 1 criterion of		PTSD: 17%
		DSM-IV BPD plus at least 2		Any anxiety disorder: 43%
		subthreshold-level criteria		Any SUD: 3%
				Any eating disorder: 8%
				BPD: 20%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Ougrin et al, 2013121	Mean age (SD):	Ages 12 to 18 years, not	Gross reality distortion, moderate	Emotional disorder
Ougrin, 2011 ²⁰⁴	IG1: 15.5 (1.2)		or severe learning disability, lack of	
SRCTN 81605131	CG: 15.6 (1.5)		fluent English, immediate risk of	CG: 22 (63)
		self-harmed and been	violence or suicide, and the need	Disruptive disorder
	N (%) Female:	referred for a psychosocial	for inpatient psychiatric admission	IG1: 5 (14)
	IG1: 28 (80)	assessment		CG: 4 (11)
	CG: 28 (80)			
	Race/Ethnicity:			
	White			
	IG1: 20 (57)			
	CG: 17 (49)			
	Black			
	IG1: 7 (20)			
	CG: 7 (20)			
	Asian			
	IG1: 1 (3)			
	CG: 7 (20)			
	Mixed			
	IG1: 6 (17)			
	CG: 3 (9)			
	Other			
	IG1: 1 (3)			
	CG: 1 (3)			

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Pineda et al, 2013 ¹²⁵ ACTRN12613000668707	Mean age (SD):		Psychoses, developmental disorders, or presented with poisoning from excessive use of recreational drugs	NR
Rossouw et al, 2012 ¹²⁸ ISRCTN95266816	Mean age (SD): IG1: 15.4 (1.3) CG: 14.8 (1.2) N (%) Female: 68 (85) Race/Ethnicity: White: 60 (75) Black: 4 (5) Asian: 8 (10) Mixed race: 6 (7.5) Other: 2 (3)	presented with at least 1 episode of confirmed self- harm within the past month, and for whom self-harm was	Comorbid diagnosis of psychosis, severe learning disability (IQ <65), pervasive developmental disorder, chemical dependence, or eating disorder in the absence of self-harm	Attempted suicide: 80% Taken overdose: 64% History of cutting: 95% Alcohol problems: 44% Substance misuse: 28% Depression: 97% Borderline personality disorder: 73%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Tang et al, 2009 ¹⁴⁴	Mean age (SD): IG1: 15.3 (1.7) CG: 15.2 (1.7) N (%) Female: IG1: 23 (66) CG: 25 (66)	attempt (BSS score >0), moderate—severe anxiety (BAI score >16), or significant	suspected axis II personality disorder, drug abuse, serious medication condition, acted out lethal suicidal behaviors, lacked proper care for suicidal risk by their	NR
	Race/Ethnicity: NR	the preceding 2 weeks followed by structured clinical interview to confirm pyshicatric diagnosis on the DSM-IV-TR		
Wood et al, 2001 ¹⁵⁹	Mean age (SD): IG1: 14.2 (1.1) CG: 14.3 (2.1) N (%) Female: IG1: 25 (78) CG: 24 (77)	to child and adolescent mental health service following an incident of deliberate self-harm, and deliberately harmed themselves on at least one	Judged too suicidal for ambulatory care, could not attend the groups, suffered from a psychotic disorder, or was unlikely to benefit from a group intervention (e.g., learning problems)	MDD: 83% Conduct or oppositional disorder: 67% Used drugs at least weekly: 44% Intoxicated at least weekly: 36%
	Race/Ethnicity: NR	other occasion during the previous year		

Abbreviations: BAI=Beck Anxiety Inventory; BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; BHS=Beck Hopelessness Scale; BPD=borderline personality disorder; BSS=Beck Scale for Suicide Ideation; CAMHS=Child and Adolescent Mental Health Services; CG=control group; C-SSRS=Columbia Suicide Severity Rating Scale; DISC-IV=Diagnostic Interview Schedule for Children-Version IV; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision; IG=intervention group; IQ=intelligence quotient; KQ=key question; MDD=major depressive disorder; MH-OAT=Mental Health Outcomes and Assessment Tools; N=number; NIMH=National Institute of Mental Health; NR=not reported; NSSI=non-suicidal self-injury; PTSD=post-traumatic stress disorder; SA=suicide attempt; SD=standard deviation; SH=self-harm; SIOJR=Suicidal Ideation Questionnaire-Junior; SRS=suicide risk screen; SUD=substance use disorder.

Appendix I Table 7. Suicide Risk Treatment Studies: Suicide Death Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Mehlum et al, 2014 ¹¹⁵	IG1: DBT (N=39)	Suicides, 19 weeks (posttreatment), ITT (IG1=39; CG=38), N (%)
Mehlum et al, 2016 ²⁰¹	CG: Enhanced usual care (N=38)	IG1: 0 (0)
Mehlum et al, 2019 ²⁰²		CG: 0 (0)
Haga et al, 2018 ²⁰³		
NCT00675129		Suicides, 3 years, mITT (IG1=37; CG=34), N (%)
		IG1: 0 (0)
		CG: 0 (0)
King et al, 2009 ¹⁰⁸	IG1: Youth-Nominated Support Team (N=223)	Suicide deaths, 12 months, analyzed (IGI=175; CG=171), N
NCT00071617	CG: TAU (N=225)	IG1: 0
		CG: 1
		P=NR
Green et al, 201193	IG1: Group psychotherapy (N=183)	Suicide deaths, 12 months, analyzed (IG1=180; CG=180), N (%)
ISRCTN 20496110	CG: Routine care (N=183)	IG1: 0 (0)
		CG: 0 (0)

Abbreviations: CG=control group; DBT=dialectical behavior therapy; IG=intervention group; KQ=key question; mITT=modified intent to treat; N=number; ITT=intent to treat; NR=not reported; TAU=treatment as usual.

Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Asarnow et al, 2017 ⁶⁶ NCT00692302	IG1: CBT (N=20) CG: TAU (N=22)	% of participants with suicide attempt, 3 months, ITT (IG1=20; CG: 22), n (%) IG1: 0 (0) CG: 4 (18.2) Z=2.45; p=0.01 favoring CBT (based on survival analysis) % of participants with suicide attempt, 5 months, ITT (IG1=20; CG: 22), n (%) IG1: 1 (5.0) CG: 4 (18.2) p=NR
		NSSI, 3 months, ITT (IG1=20; CG: 22), probabilities of survival without (SE) IG1: 0.55 (0.11) CG: 0.43 (0.14) p=0.054 favoring CBT (based on survival analyses)
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	IG1: Family therapy (N=415) CG: TAU (N=417)	Self-harm events per participant, 36 months, ITT (IG=415; CG=417), mean (SD) IG1: 1.0 (2.19) CG: 1.2 (3.22) P NR
		SASII self-harm event, 12 to 18 months; mITT (IG=268; CG=210), n (%) IG1: 202 (75) CG: 147 (70) P NR

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Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Green et al, 2011 ⁹³ ISRCTN 20496110	IG1: Group psychotherapy (N=183) CG: Routine care (N=183)	Frequency of self-harm, 0 to 6 months, analyzed (IG1=181; CG=181), geometric mean IG1: 4.6 CG: 4.4 Ratio: 1.01 (95% CI, 0.80 to 1.29); P=0.91 Frequency of self-harm, 6 to 12 months, analyzed (IG1=179; CG=180), geometric mean IG1: 2.0 CG: 2.1 Ratio: 0.94 (95% CI, 0.73 to 1.18); P=0.60 Severity of self-harm, 0 to 6 months and 6 to 12 months, analyzed (IG1=181; CG=181), N No problem IG1: 37, 75 CG: 40, 70 Mild problem IG1: 96, 68 CG: 79, 76 Marked problem IG1: 27, 24 CG: 37, 21 Severe problem IG1: 27, 11 CG: 25, 13 Proportional OR, 0 to 6 months (95% CI): 0.81 (0.54 to 1.20); P=0.29 Proportional OR, 6 to 12 months (95% CI): 0.94 (0.63 to 1.40); P=0.75 Both adjusted for site, sex, age, frequency and severity of self-harm at baseline, psychosocial risk, behavioral disorder, and depressive disorder Self-harm resulting in injury, 12 months, analyzed (IG1=180; CG=180), N (%) IG1: 1 (0.05) CG: 2 (1.1) Time to self-harm, 0 to 12 months, N analyzed NR, median (IQR) IG1: 37 days (15 to 123) CG: 49 days (17 to 184)

Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Griffiths et al, 2019 ⁹⁴ NCT02771691	IG1: MBT (N=26) CG: TAU (N=27)	Self-harm subscale (RTSHI), 12 weeks (posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 26.00 (12.57) CG: 23.12 (12.28)
		Self-harm subscale (RTSHI), 24 weeks (12 week posttreatment) ITT (IG1=22; CG=26), mean (SD) IG1: 24.41 (12.52) CG: 22.93 (12.35)
		Self-harm subscale (RTSHI), 36 weeks (24 week posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 24.50 (13.88) CG: 22.74 (13.04) Time x Group interaction (presumably across all 3 followup timepoints): P=NS
		RTSHI total, 12 weeks (posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 38.78 (19.65) CG: 36.00 (18.80)
		RTSHI total, 24 weeks (12 week posttreatment) ITT (IG1=22; CG=26), mean (SD) IG1: 37.24 (20.22) CG: 36.14 (19.67) Time x Treatment interaction: P=NS
		RTSHI total, 36 weeks (24 week posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 37.16 (21.90) CG: 36.03 (19.91) Time x Treatment interaction: P=NS
		Time x Treatment interaction. P=NS Time x Group interaction (presumably across all 3 followup timepoints): P=NS
Hazell et al, 2009 ⁹⁵ ACTRN12608000532303		Engaged in repetition of self-harm, 6 to 12 months, analyzed (IG1=34; CG=34), N (%) IG1: 30 (88) CG: 24 (71) Chi-square=3.24 P=0.07
King et al, 2009 ¹⁰⁸ NCT00071617	IG1: Youth-Nominated Support Team (N=223) CG: TAU (N=225)	Suicide attempt, 12 months, analyzed (IGI=175; CG=171), N IG1: 29 CG: 35 Chi-square=0.44 P=0.51

Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³ NCT00675129	IG1: DBT (N=39) CG: Enhanced usual care (N=38)	Self-harm episodes, 19 weeks (posttreatment), ITT (IG1=39; CG=38), mean (95% CI) IG1: 9.0 (4.8 to 13.2) CG: 22.5 (11.4 to 33.5) Between-group difference NR; P<0.05
		Self-harm episodes, posttreatment to 1 year, mITT (IG1=38; CG=37), mean (95% CI) IG1: 5.5 (1.7 to 9.1) CG: 14.8 (7.3 to 22.3) Between-group difference NR; P<0.05
		Self-harm episodes, between 1 and 3 years, mITT (IG1=37; CG=34), mean (SD) IG1: 6.32 (12.35) CG: 18.94 (42.74) P=NR
		Self-harm episodes, between 1 and 3 years, mITT(IG1=37; CG=34), median (range, IQR) IG1: 1 (0 to 65, 18) CG: 5 (0 to 226, 7) P<0.001 for comparison of ranges
		Self-harm episodes, 3 years, mITT(IG1=37; CG=34), IRR (95% CI) IRR, 0.32 (0.13 to 0.80); P=0.015 (favoring intervention) Adjusted IRR, 0.46 (0.18 to 1.19); P=0.108 adjusting for gender, suicide attempt in last 4 months at baseline, and presence of a depressive order at baseline
Rossouw et al, 2012 ¹²⁸ ISRCTN95266816	IG1: Mentalization-based treatment for adolescents (MBT-A) (N=40) CG: TAU (N=40)	Self-harm (RTSHI), 12 months, ITT (IG1=40; CG=40), log mean (SE) IG1: 1.33 (0.22) CG: 2.01 (0.21) Group differences from mixed-effects random regression model at 12 months, P<0.01 favoring MBT-A
		Odds of reporting at least one incident of self-harm, 12 months, completers (IG1=36; CG=35), n (%) IG1: 22 (56) CG: 33 (83) P=0.01, favoring MBT-A

Author, Year, Registry Number	Treatment Interventions and Comparators	Outcome
Wood et al, 2001 ¹⁵⁹	IG1: Developmental Group Therapy (N=32) CG: Treatment as usual (N=31)	Number of episodes of deliberate self-harm, 7 months (posttreatment), ITT (IGI=32; CG=31), mean (95% CI) IG1: 0.6 (0.3 to 0.9) CG: 1.8 (0.6 to 3.0) P=NR Number of persons repeating self-harm, 7 months (posttreatment), ITT (IG1=32; CG=31), N (%) IG1: 2 (6) CG: 10 (32) OR: 6.3 (1.4 to 28.7) Mean time in weeks to first repeated episode of self-harm, 7 months (posttreatment), ITT (IG1=32; CG=31), Mean (SD) IG1: 11.9 (7.2)
		CG: 7 (6.3) Mean difference, 4.9 (95% CI, 0.0 to 9.8); P<0.05

Abbreviations: CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; DBT=dialectical behavior therapy; HR=hazard ratio; IG=intervention group; IQR=interquartile ratio; ITT=intent to treat; KQ=key question; MBT=mentalization-based treatment; MBT-A=mentalization-based treatment for adolescents; mITT=modified intent to treat; NR=not reported; NS=not significant; NSSI=non-suicidal self-injury; OR=odds ratio; RTSHI=Risk-Taking and Self-Harm Inventory for Adolescents; SASII=Suicide Attempt Self-Injury Interview; SD=standard deviation; SE=standard error; TAU=treatment as usual.

Appendix I Table 9. Suicide Risk Treatment Studies: Suicide-Related Hospitalization or Emergency Department Use Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	IG1: Family therapy (N=415) CG: TAU (N=417)	Hospital attendance for self-harm event, 18 months, ITT (IG=415; CG=417), N (%) IG1: 118 (28) CG: 103 (25) HR (95% CI): 1.14 (0.87 to 1.49); P=0.33
		Hospital attendance for self-harm event, 12 months, ITT (IG=415; CG=417), N (%) IG1: NR CG: NR HR (95% CI): 1.09 (0.81 to 1.48); P=0.56
		Hospital attendance for self-harm event, 36 months, ITT (IG=415; CG=417), N (%) IG1: 168 (40.5) CG: 166 (39.8) HR (95% CI): 1.03 (0.83 to 1.28); P=0.78
Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹ Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³ NCT00675129	IG1: DBT (N=39) CG: Enhanced usual care (N=38)	Admitted to hospital due to self-harm, 19 weeks (posttreatment), ITT (IG1=39; CG=38), N (%) IG1: 1 (2) CG: 2 (5) P=NS
		ER visit due to self-harm, 19 weeks (posttreatment), ITT (IG1=39; CG=38), N (%) IG1: 2 (5) CG: 5 (13) P=NS
Ougrin et al, 2013 ¹²¹ Ougrin, 2011 ²⁰⁴ ISRCTN 81605131	IG1: Therapeutic Assessment (N=35) CG: Assessment as usual (N=35)	One or more presentation to A&E with self-harm, 2 years, ITT (IG1=35; CG=34), N (%) IG1: 7 (20) CG: 9 (26) OR: 0.69 (0.23 to 2.13); P=0.53

Appendix I Table 9. Suicide Risk Treatment Studies: Suicide-Related Hospitalization or Emergency Department Use Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Griffiths et al, 2019 ⁹⁴ NCT02771691	IG1: MBT (N=26) CG: TAU (N=27)	Self-harm ED presentation, 12 weeks (posttreatment), ITT (IG1=22; CG=26), mean number (range) IG1: 0.36 (0 to 2) CG: 0.23 (0 to 2)
		Self-harm ED presentation, 24 weeks (12 week posttreatment), ITT (IG1=22; CG=26), mean number (range) IG1: 0.23 (0 to 2) CG: 0.54 (0 to 3)
		Self-harm ED presentation, 36 weeks (24 week posttreatment), ITT (IG1=22; CG=26), mean number (range) IG1: 0.09 (0 to 1) CG: 0.35 (0 to 4)
		Time x Group interaction (presumably across all 3 followup timepoints): P=NS

Abbreviations: A&E=accident and emergency; CG=control group; CI=confidence interval; DBT=dialectical behavior therapy; ED=emergency department; ER=emergency room; HR=hazard ratio; IG=intervention group; ITT=intent to treat; KQ=key question; MBT=mentalization-based treatment; NR=not reported; NS=not significant; OR=odds ratio; TAU=treatment as usual.

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰	IG1: Family therapy (N=415) CG: TAU (N=417)	BSS, 12 months, analyzed (IG=257; CG=202), mean (SD) IG1: 4.6 (7.25) CG: 5.7 (7.91)
ISRCTN59793150		BSS, 18 months, analyzed (IG=212; CG=180), mean (SD) IG1: 4.6 (7.76) CG: 5.2 (7.76)
		BSS, 12 months, analyzed (IG=257; CG=202), proportion with ideation, N (%) IG1: 111 (43.2) CG: 98 (48.5)
		BSS, 18 months, analyzed (IG=212; CG=180), proportion with ideation, N (%) IG1: 85 (40.1) CG: 80 (44.4)
		BSS, 12 months, ITT (IG=415; CG=417), proportion with ideation (SE %) IG1: 0.26 (0.05) CG: 0.36 (0.05) OR (95% CI): 0.64 (0.44 to 0.94); P=0.024
		BSS, 18 months, ITT (IG=415; CG=417), proportion with ideation (SE %) IG1: 0.22 (0.04) CG: 0.28 (0.05) OR (95% CI): 0.76 (0.49 to 1.16); P=0.20
		HSFC, 12 months, ITT (IG=415; CG=417) mean (SE) IG1: 4.8 (0.40) CG: 5.1 (0.43) Difference, mean (95% CI), SE: -0.3 (-1.1 to 0.4), 0.37; P=0.38
		HSFC, 18 months, ITT (IG=415; CG=417) mean (SE) IG1: 4.4 (0.42) CG: 4.6 (0.43) Difference, mean (95% CI), SE: -0.2 (-0.9 to 0.5), 0.36; P=0.63

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Diamond et al, 2010 ⁸² NCT00604097	IG1: Attachment-Based Family Therapy (N=35) CG: Enhanced Usual Care (N=31)	SIQ-Jr, 12 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 5.2 (1.6 to 8.8) CG: 16.2 (10.1 to 22.2) P=NR
		SIQ-Jr, 24 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 10.4 (5.6 to 15.2) CG: 23.0 (15.6 to 30.4) P=NR Difference in difference from baseline to followup: 2.03 (SE=0.59), effect size=0.97, in favor of IG1, (t(64=-3.45, p=0.001)
		SSI, 12 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 69.2 (50.2 to 88.2) CG: 34.6 (15.0 to 54.2) P=NR
		SSI, 24 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 82.1 (67.0 to 97.3) CG: 46.2 (25.6 to 66.7) P=NR Difference in difference from baseline to followup: 2.07 (SE=0.80), effect size=0.64, in favor of IG1, (t(64=2.58, p=0.012)
Green et al, 2011 ⁹³ ISRCTN 20496110	IG1: Group psychotherapy (N=183) CG: Routine care (N=183)	SIQ, mean difference at 6 months, analyzed (IGI=171; CG=179), mean difference (95% CI) 0.07 (-8.60 to 8.75), P=0.99
		SIQ, mean difference at 12 months, analyzed (IGI=169; CG=174), mean difference (95% CI) -2.37 (-11.11 to 6.36), P=0.59
Hazell et al, 2009 ⁹⁵ ACTRN12608000532303	IG1: Group therapy (N=35) CG: Routine care (N=37)	SIQ, 8 weeks, analyzed (IG1=34; CG=37), mean (SD) IG1: 74.11 (41.75) CG: 76.40 (54.28)
		SIQ, 12 months, analyzed (IG1=34; CG=37), mean (SD) IG1: 59.78 (42.07) CG: 61.68 (49.62) F=0.07 P=0.80 (for group differences from baseline)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Hill et al, 2019 ⁹⁷ NR	IG1: Internet CBT (N=40) CG: Information-only control (N=40)	BSS 2 weeks (posttreatment), mITT (IG1=41; CG=39), mean (SD) IG1: 2.05 (3.27) CG: 4.49 (6.01) P=0.12
		BSS, 8 weeks, mITT (IG1=41; CG=39), mean (SD) IG1: 1.69 (3.01) CG: 2.57 (4.40) P=0.92
		Perceived Burdensomeness, 2 weeks (posttreatment), mITT (IG1=41; CG=39), mean (SD) IG1: 17.76 (6.37) CG: 18.81 (6.26) P=0.26
		Perceived Burdensomeness, 8 weeks, mITT (IG1=41; CG=39), mean (SD) IG1: 13.90 (6.86) CG: 15.85 (6.25) P=0.10
		Thwarted Belongingness, 2 weeks (posttreatment), mITT (IG1=41; CG=39), mean (SD) IG1: 31.78 (7.32) CG: 35.22 (8.60) P=0.12
		Thwarted Belongingness, 8 weeks, mITT (IG1=41; CG=39), mean (SD) IG1: 27.30 (8.42) CG: 31.76 (8.09) P=0.03
Hooven et al, 2012 ¹⁰⁰	IG1: C-Care (N=153) IG2: P-CARE (N=155) IG3: C-Care + P-Care (N=164) CG: TAU (N=143)	Suicide ideation, change from baseline to 1 month, ITT (IG1=153; CG=143), rate of change coefficients IG1: -1.131 CG: -0.917 P=NS, 1 tailed test
		Suicide ideation, change from baseline to 1 month, ITT (IG2=155; CG=143), rate of change coefficients IG2: -1.033 CG: -0.917 P=NS, 1 tailed test

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Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Hooven et al, 2012 ¹⁰⁰ (continued)		Suicide ideation, change from baseline to 1 month, ITT (IG3=164; CG=143), rate of change coefficients IG3: -1.451 CG: -0.917 P<0.001, 1 tailed test, favoring IG3 (C+P care)
		Suicide ideation, change from baseline to 9 months, ITT (IG3=164; CG=143), rate of change coefficients IG3: NR CG: NR P <0.005, 1 tailed test, favoring IG3 (C+P care)
		Direct suicide threats, change from baseline to 1 month, ITT (IG1=153; CG=143), rate of change coefficients IG1: -0.443 CG: -0.318 P=NS, 1 tailed test
		Direct suicide threats, change from baseline to 1 month, ITT (IG2=155; CG=143), rate of change coefficients IG2: -0.294 CG: -0.318 P=NS, 1 tailed test
		Direct suicide threats, change from baseline to 1 month, ITT (IG3=164; CG=143), rate of change coefficients IG3: -0.556 CG: -0.318 P<0.05, 1 tailed test
		Direct suicide threats, change from baseline to 9 months, ITT (IG3=164; CG=143), rate of change coefficients IG3: NR CG: NR P <0.01, 1 tailed test, favoring IG3 (C+P care)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
King et al, 2009 ¹⁰⁸ NCT00071617	IG1: Youth-Nominated Support Team (N=223) CG: TAU (N=225)	BHS, 6 weeks, analyzed (IGI=NR; CG=NR), adjusted mean IG1: 6.82 CG: 7.80 Main effects mixed model, P=0.09
		BHS, 3 months, analyzed (IGI=168; CG=174), adjusted mean IG1: 6.72 CG: 6.53 Main effects mixed model, P=0.98
		BHS, 12 months, analyzed (IGI=175; CG=171), adjusted mean IG1: 4.37 CG: 5.08 Main effects mixed model, P=0.14
		SIQ-Jr, 6 weeks, analyzed (IGI=NR; CG=NR), adjusted mean IG1: 25.55 CG: 29.71 Main effects mixed model, P=0.04, Cohen's d=0.21
		SIQ-Jr, 3 months, analyzed (IGI=168; CG=174), adjusted mean IG1: 23.62 CG: 21.57 Main effects mixed model, P=0.26
		SIQ-Jr, 12 months, analyzed (IGI=175; CG=171), adjusted mean IG1: 16.71 CG: 17.14 Main effects mixed model, P=0.77 All of the above means were adjusted for baseline CDRS-R score, alcohol and
		drug use problem severity, and baseline scores for the outcome being measured
King et al, 2015 ¹⁰⁷ NR	IG1: Teen Option to Change (Motivational Interviewing) (N=27) CG: Enhanced TAU (N=22)	SIQ-Jr, 2 months, ITT (IG1=24; CG=22), mean (SD) IG1: 21.46 (17.4) CG: 24.28 (17.3) Cohen's d=0.22 P for time x treatment interaction=NS
		BHS, 2 months, ITT (IG1=24; CG=22), mean SD IG1: 5.66 (5.2) CG: 8.64 (5.7) Cohen's d=0.40 P for time x treatment interaction=NS

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Mehlum et al, 2014 ¹¹⁵	IG1: DBT (N=39)	SIQ-Jr, 71 weeks, mITT (IG1=38; CG=37), mean (SD)
Mehlum et al, 2016 ²⁰¹	CG: Enhanced usual care (N=38)	IG1: 20.45 (19.15)
Mehlum et al, 2019 ²⁰²		CG: 22.05 (21.86)
Haga et al, 2018 ²⁰³ NCT00675129		Between-group difference in slope=0.15; P=0.110
		SIQ-Jr, 3.1 years, mITT(IG1=37; CG=34), mean (SD)
		IG1: 19.64 (18.54)
		CG: 23.15 (18.12)
		Between-group difference in slope=0.099; P=0.111
		Between-group difference in mean change=NR; P=0.430
		BHS, 19 weeks (posttreatment), ITT (IG1=39; CG=38), mean (SD)
		IG1: 6.23 (5.30)
		CG: 9.06 (6.53)
		Between-group difference in slope=-0.13; P=0.071
		BHS, 71 weeks, mITT (IG1=38; CG=37), mean (SD)
		IG1: 6.97 (5.66)
		CG: 7.26 (6.57)
		Between-group difference in slope=0.02; P=0.446
		BHS, 3.1 years, mITT (IG1=37; CG=34), mean (SD)
		IG1: 6.16 (5.24)
		CG: 8.10 (5.76)
		Between-group difference in slope=0.006; P=0.762 Between-group difference in mean change=NR; P=0.154
Pineda et al, 2013 ¹²⁵	IG1: RAP-P (Family Intervention) (N=24)	ASQ-R, posttreatment, completers (IG1=22; CG=18), mean (SD)
ACTRN12613000668707	CG: Routine care (N=24)	IG1: 8.73 (4.88)
		CG: 11.89 (5.47)
		ASQ-R, 6 months, completers (IG1=22; CG=18), mean (SD)
		IG1: 6.77 (4.06)
		CG: 10.83 (5.33)
		Time x Group interaction (presumably across both timepoints): P=0.05, favoring RAP-P

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Tang et al, 2009 ¹⁴⁴	IG1: IPT-A-IN (N=35) CG: TAU (N=38)	BHS, 6 weeks, ITT (IG1=35; CG=38), mean (SD) IG1: 7.74 (5.29) CG: 12.42 (4.08) P<0.01 for post comparison controlling for baseline score
		BSS, 6 weeks, ITT (IG1=35; CG=38), mean (SD) IG1: 8.97 (10.77) CG: 16.29 (7.99) P<0.01 for post comparison controlling for baseline score
Wood et al, 2001 ¹⁵⁹	IG1: Developmental Group Therapy (N=32) CG: Treatment as usual (N=31)	SIQ, change from baseline to 7 months (posttreatment), analyzed (IG1=28; CG=27), mean (SD) IG1: 47.3 (50.5) CG: 39.7 (46.7) Mean difference (95% CI): 7.5 (-18.8 to 33.9)

Abbreviations: ASQ-R=Adolescent Suicide Questionnaire—Revised; BHS=Beck Hopelessness Scale; BSS=Beck Scale for Suicide Ideation; CBT=cognitive behavioral therapy; C-CARE=Counselors Care, Assess, Respond, Empower; CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; CI=confidence interval; DBT=dialectical behavior therapy; HR=hazard ratio; HSFC=Hopelessness Scale for Children; IG=intervention group; IPT-A-IN=intensive interpersonal psychotherapy for depressed adolescents with suicidal risk; ITT=intent to treat; KQ=key question; mITT=modified intent to treat; N=number; NR=not reported; NS=not significant; OR=odds ratio; P-CARE=Parents-Counselors Care, Assess, Respond, Empower; RAP-P=Resourceful Adolescent Parent Program; SD=standard deviation; SE=standard error; SIQ=Suicidal Ideation Questionnaire; SIQ JR=Suicidal Ideation Questionnaire as usual.

Author, Year,	Treatment Interventions	
Registry Number Griffiths et al, 201994	and Comparators IG1: MBT (N=26)	Anxiety Symptoms RCADS Anx, 12 weeks (posttreatment), ITT (IG1=22; CG=26), mean (SD)
NCT02771691	CG: TAU (N=27)	IG1: 78.21 (21.48)
NC102111091	CG. TAU (N=21)	CG: 65.42 (22.4)
		00.00.42 (22.4)
		RCADS Anx, 24 weeks (12 week posttreatment), ITT (IG1=22; CG=26), mean (SD)
		IG1: 76.56 (25.24)
		CG: 67.14 (22.05)
		RCADS Anx, 36 weeks (24 week posttreatment), ITT (IG1=22; CG=26), mean (SD)
		IG1: 77.55 (24.91)
		CG: 68.4 (21.61)
		Time x Group interaction (presumably across all 3 followup timepoints): P=NS
Hooven et al, 2012100	IG1: C-Care	4 anxiety items, change from baseline to 1 month, ITT (IG1=153; CG=143), rate of change coefficients
	(N=153)	IG1: -0.683
	IG2: P-CARE	CG: -0.440
	(N=155)	P<0.05, 1 tailed test, favoring IG1 (C care)
	IG3: C-Care +	A sociate items about from heavilies to A sociate ITT (100, 455, 00, 440), and of about a sociation to
	P-Care (N=164)	4 anxiety items, change from baseline to 1 month, ITT (IG2=155; CG=143), rate of change coefficients
	CG: TAU (N=143)	IG2: -0.515 CG: -0.440
		P=NS, 1 tailed test
		F=NO, I talled test
		4 anxiety items, change from baseline to 1 month, ITT (IG3=164; CG=143), rate of change coefficients
		IG3: -0.849
		CG: -0.440
		P<0.001, 1 tailed test, favoring IG3 (C+P care)
		4 anxiety items, change from baseline to 2.5 months, ITT (IG3=164; CG=143), rate of change coefficients
		IG3: NR
		CG: NR
		P <0.006, 1 tailed test, favoring IG3 (C+P care)
Tang et al, 2009144	IG1: IPT-A-IN	BAI, 6 weeks, ITT (IG1=35; CG=38), mean (SD)
	(N=35)	IG1: 11.94 (10.34)
	CG: TAU (N=38)	CG: 25.45 (14.35)
		F=21.79
		P<0.001 (favoring intervention)

Abbreviations: BAI=Beck Anxiety Inventory; C-CARE=Counselors Care, Assess, Respond, Empower; CG=control group; IG=intervention group; IPT-A-IN=intensive interpersonal psychotherapy for depressed adolescents with suicidal risk; ITT=intent to treat; KQ=key question; MBT=mentalization-based treatment; NR=not reported; NS=not significant; P-CARE=Parents-Counselors Care, Assess, Respond, Empower; RCADS=Revised Children's Anxiety and Depression Scale; SD=standard deviation; TAU=treatment as usual.

Appendix I Table 12. Suicide Risk Treatment Studies: Depression-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	IG1: Family therapy (N=415) CG: TAU (N=417)	CDRS-R, posttreatment 12 months, analyzed (IG=244; CG=187), mean (SE) IG1: 36.5 (14.33) CG: 37.2 (13.09) CDRS-R, posttreatment 18 months, analyzed (IG=204; CG=165), mean (SE) IG1: 33.8 (14.77) CG: 35.0 (14.39) CDRS-R, posttreatment 12 months, ITT (IG=248; CG=189), mean (SE) IG1: 33.2 (1.46) CG: 33.9 (1.57) Difference, mean (95% CI), SE=-0.6 (-3.1 to 1.9), 1.27 P=0.62 CDRS-R, posttreatment 18 months, ITT (IG=204; CG=165), mean (SE) IG1: 30.6 (1.50) CG: 31.6 (1.46) Difference, mean (95% CI), SE=-1.0 (-3.5 to 1.5), 1.26
Diamond et al, 2010 ⁸² NCT00604097	IG1: Attachment-Based Family Therapy (N=35) CG: Enhanced Usual Care (N=31)	P=0.43 BDI-II, 12 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 12.6 (8.0 to 17.2) CG: 18.5 (12.9 to 24.0) P=NR BDI-II, 24 weeks, ITT (IG1=35; CG=31), mean (95% CI) IG1: 12.4 (7.8 to 16.9) CG: 16.2 (10.4 to 21.9) P=NR BDI-II <9, 12 weeks, analyzed (IG1=31; CG=29), N (%) IG1: 17 (55) CG: 9 (31) OR: 2.70 (0.94 to 7.71); P=0.06 BDI-II <9, 24 weeks, analyzed (IG1=31; CG=26), N (%) IG1: 18 (58) CG: 10 (38) OR: 2.21 (0.76 to 6.42); P=0.14

Appendix I Table 12. Suicide Risk Treatment Studies: Depression-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Green et al, 2011 ⁹³ ISRCTN 20496110	IG1: Group psychotherapy (N=183) CG: Routine care (N=183)	MFQ, mean difference at 6 months, analyzed (IGI=171; CG=178), mean difference (95% CI) -0.44 (-3.49 to 2.61), P=0.78 MFQ mean difference at 12 months, analyzed (IGI=170; CG=174), mean difference (95% CI)
Griffiths et al, 2019 ⁹⁴ NCT02771691	IG1: MBT (N=26) CG: TAU (N=27)	-1.45 (-4.90 to 1.99), P=0.41 RCADS MD, 12 weeks (posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 20.39 (4.74) CG: 18.15 (6.57)
		RCADS MD, 24 weeks (12 week posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 19.89 (5.64) CG: 17.81 (6.65)
		RCADS MD, 36 weeks (24 week posttreatment), ITT (IG1=22; CG=26), mean (SD) IG1: 20.07 (5.72) CG: 18.49 (6.96) Time x Group interaction (presumably across all 3 followup timepoints): P=NS
Hazell et al, 2009 ⁹⁵ ACTRN12608000532303	IG1: Group therapy (N=35) CG: Routine care (N=37)	MFQ, 8 weeks, analyzed (IG1=34; CG=37), mean (SD) IG1: 30.91 (17.25) CG: 32.38 (19.94)
		MFQ, 12 months, analyzed (IG1=34; CG=37), mean (SD) IG1: 27.40 (17.16) CG: 31.76 (18.91) F=0.27 P=0.60 (presumably across 2 timepoints)
Hill et al, 2019 ⁹⁷ NR	IG1: Internet CBT (N=40) CG: Information-only control (N=40)	RADS-2, 2 weeks (posttreatment), mITT (IG1=41; CG=39), mean (SD) IG1: 23.12 (4.50) CG: 24.64 (5.90) P=0.45
		RADS-2, 8 weeks (posttreatment), mITT (IG1=41; CG=39), mean (SD) IG1: 20.93 (4.49) CG: 23.00 (5.41) P=0.07

Appendix I Table 12. Suicide Risk Treatment Studies: Depression-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Hooven et al, 2012 ¹⁰⁰	IG1: C-Care (N=153) IG2: P-CARE (N=155) IG3: C-Care + P-Care (N=164) CG: TAU (N=143)	CES-D, change from baseline to 1 month, ITT (IG1=153; CG=143), rate of change coefficients IG1: -0.951 CG: -0.685 P<0.01, 1 tailed test, favoring IG1 (C-care) CES-D, change from baseline to 1 month, ITT (IG1=155; CG=143), rate of change coefficients IG2: -0.815 CG: -0.685 P=NS, 1 tailed test CES-D, change from baseline to 1 month, ITT (IG1=164; CG=143), rate of change coefficients IG3: -1.021
King et al, 2009 ¹⁰⁸ NCT00071617	IG1: Youth-Nominated Support Team (N=223) CG: TAU (N=225)	CG: -0.685 P<0.01, 1 tailed test, favoring IG3 (C+P care) CDRS-R, 6 weeks, analyzed (IGI=NR; CG=NR), adjusted mean IG1: 39.69 CG: 40.80 Main effects mixed model, P=0.40 CDRS-R, 3 months, analyzed (IGI=168; CG=174), adjusted mean IG1: 38.27 CG: 38.55 Main effects mixed model, P=0.84 CDRS-R, 12 months, analyzed (IGI=175; CG=171), adjusted mean
King et al, 2015 ¹⁰⁷ NR	IG1: Teen Option to Change (Motivational Interviewing) (N=27) CG: Enhanced TAU (N=22)	IG1: 33.16 CG: 33.96 Main effects mixed model, P=0.52 RADS-2-SF, 2 months, ITT (IG1=24; CG=22), mean (SD) IG1: 25.38 (4.7) CG: 30.87 (4.0) Cohen's d=1.07 P<0.01 for time x treatment interaction

Author, Year, Registry	Treatment Interventions	Danners in Committees
Number	and Comparators	Depression Symptoms
Mehlum et al, 2014 ¹¹⁵ Mehlum et al, 2016 ²⁰¹	IG1: DBT (N=39) CG: Enhanced usual care	SMFQ, 19 weeks (posttreatment), ITT (IG1=39; CG=38), mean (SD) IG1: 10.19 (5.04)
Mehlum et al, 2019 ²⁰²	(N=38)	CG: 12.58 (6.62)
Haga et al, 2018 ²⁰³	(N=30)	Between-group difference in slope=-0.10; P=0.179
NCT00675129		Between-group difference in slope=-0.10, 1 =0.179
140100073123		SMFQ, 71 weeks, mITT (IG1=38; CG=37), mean (SD)
		IG1: 9.88 (5.53)
		CG: 9.19 (6.57)
		Between-group difference in slope=0.04; P=0.240
		SMFQ, 3.1 years, mITT (IG1=37; CG=34), mean (SD)
		IG1: 9.54 (5.3)
		CG: 10.56 (6.3)
		Between-group difference in slope=0.011; P=0.556
		Between-group difference in mean change=NR; P=0.471
		MADRS, 19 weeks (posttreatment), ITT (IG1=39; CG=38), mean (SD)
		IG1: 12.29 (7.52)
		CG: 15.76 (8.14)
		Between-group difference in change in slope=-0.22; P=0.019
		MADRS, 71 weeks, mITT (IG1=38; CG=37), mean (SD)
		IG1: 15.09 (8.08)
		CG: 15.73 (9.06)
		Between-group difference in slope=0.06; P=0.199
		MADRS, 3.1 years, mITT (IG1=37; CG=34), mean (SD)
		IG1: 11.7 (7.2)
		CG: 10.33 (7.03)
		Between-group difference in slope=0.044; P=0.089 Between-group difference in mean change=NR; P=0.429
Rossouw et al, 2012 ¹²⁸	IG1: Mentalization-based	MFQ, 12 months, ITT (IG1=40; CG=40), log mean (SE)
ISRCTN95266816	treatment for adolescents	IG1: 9.26 (1.27)
	(MBT-A) (N=40)	CG: 11.54 (1.14)
	CG: TAÚ (N=40)	Group differences from mixed-effects random regression model at 12 months, P<0.05 favoring
		MBT-A
Tang et al, 2009144	IG1: IPT-A-IN (N=35)	BDI-II, 6 weeks, ITT (IG1=35; CG=38), mean (SD)
	CG: TAU (N=38)	IG1: 19.97 (14.68)
		CG: 31.58 (12.01)
		F=15.64
		P<0.001 (favoring intervention)

Appendix I Table 12. Suicide Risk Treatment Studies: Depression-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Wood et al, 2001 ¹⁵⁹	IG1: Developmental Group	MFQ, change from baseline to 7 months (posttreatment), analyzed (IG1=29; CG=27), mean (SD)
	Therapy (N=32)	IG1: 18.8 (16.0)
	CG: Treatment as usual	CG: 15.3 (13.0)
	(N=31)	Mean difference (95% CI): 3.5 (-4.4 to 11.3)

Abbreviations: BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; C-CARE=Counselors Care, Assess, Respond, Empower; CDRS-R=Children's Depression Rating Scale-Revised; CES-D=Center for Epidemiological Studies-Depression; CG=control group; CI=confidence interval; DBT=dialectical behavior therapy; IG=intervention group; IPT-A-IN=intensive interpersonal psychotherapy for depressed adolescents with suicidal risk; ITT=intent to treat; KQ=key question; MADRS=Montgomery-Åsberg Depression Rating Scale; MBT=mentalization-based treatment; MBT-A=mentalization-based treatment for adolescents; MFQ=mood & feelings questionnaire; mITT=modified intent to treat; N=number; NR=not reported; NS=not significant; P-CARE=Parents-Counselors Care, Assess, Respond, Empower; RADS-2=Reynolds Adolescent Depression Scale, 2nd Edition; RADS-2-SF=Reynolds Adolescent Depression Scale, 2nd Edition: Short Form; RCADS MD=Revised Children's Anxiety and Depression Scale-Depression; SD=standard deviation; SE=standard error; SMFQ=Short Mood & Feelings Questionnaire; TAU=treatment as usual.

Appendix I Table 13. Suicide Risk Treatment Studies: Response and Remission Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Presence/Absence of Diagnosis
Diamond et al, 2010 ⁸² NCT00604097	IG1: Attachment-Based Family Therapy (N=35) CG: Enhanced Usual Care (N=31)	SIQ-Jr, clinical response defined as ≤13 SSI, clinical response defined as 0 vs. 1 suicide attempt BDI-II, clinical response defined as ≤9
	CG. Efficienced Osual Care (N=51)	SIQ-Jr <13, 12 weeks, analyzed (IG1=31; CG=29), N (%) IG1: 27 (87) CG: 15 (52)
		OR: 6.30 (1.76 to 22.61); P=0.003 (favoring intervention)
		SIQ-Jr <13, 24 weeks, analyzed (IG1=30; CG=26), N (%) IG1: 21 (70)
		CG: 9 (35) OR: 4.41; P=0.008 (favoring intervention)
		SSI (0 vs. 1), 12 weeks, analyzed (IG1=26; CG=26), N (%) IG1: 18 (69) CG: 9 (35)
		OR: 4.45 (1.33 to 13.56); P=0.013 (favoring intervention)
		SSI (0 vs. 1), 24 weeks, analyzed (IG1=28; CG=26), N (%) IG1: 23 (82) CG: 12 (46)
		OR: 5.37 (1.56 to 18.49); P=0.006 (favoring intervention)
Hill et al, 2019 ⁹⁷ NR	IG1: Internet CBT (N=40) CG: Information-only control (N=40)	Meeting reliable change criteria (Jacob and Truax, 1991) with clinically significant improvement based on perceived burdensomeness scores closer to that of the healthy population mean (≤14.61)
		Treatment response, 8 weeks, mITT (IG1=41; CG=39), N (%) IG1: 10 (24.4) CG: 4 (10.2)

Abbreviations: BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CG=control group; IG=intervention group; KQ=key question; mITT=modified intent to treat; N=number; NR=not reported; OR=odds ratio; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; SSI=Scale for Suicidal Ideation.

Appendix I Table 14. Suicide Risk Treatment Studies: Functioning Outcomes (KQ 4)

	Treatment Interventions	
Author, Year, Registry Number	and Comparators	Functioning Outcomes
Cottrell et al, 2018 ⁸⁰	IG1: Family therapy (N=415)	PQ-LES, 12 months, analyzed (IG=259; CG=201), mean (SD)
Cottrell et al, 2018 ¹⁹⁹	CG: TAU (N=417)	IG1: 48.5 (10.57)
Cottrell et al, 2018 ²⁰⁰		CG: 47.3 (10.26)
ISRCTN59793150		DO LEC 40 months ITT (IC 204: CC 465) moon (CD)
		PQ-LES, 18 months, ITT (IG=204; CG=165), mean (SD) IG1: 49.1 (11.14)
		CG: 48.7 (11.25)
		CG. 46.7 (11.23)
		PQ-LES, 12 months, ITT (IG=415; CG=417), mean (SE)
		IG1: 49.9 (1.12)
		CG: 48.8 (1.13)
		Difference, mean (95% CI), SE: 1.1 (-0.5 to 2.7), 0.82; P=0.18
		PQ-LES, 18 months, ITT (IG=415; CG=417), mean (SE)
		IG1: 50.6 (1.12)
		CG: 50.4 (1.20)
		Difference, mean (95% CI), SE: 0.1 (-1.9 to 2.1), 1.02; P=0.90
		GHQ-12-Caregiver, 12 months, ITT (IG=415; CG=417), mean (SE)
		IG1: 12.8 (0.61)
		CG: 13.5 (0.65)
		Difference, mean (95% CI), SE: -0.7 (-1.8 to 0.3), 0.54; P=0.19
		GHQ-12-Caregiver, 18 months, ITT (IG=415; CG=417), mean (SE)
		IG1: 12.8 (0.61)
		CG: 13.5 (0.65)
		Difference, mean (95% CI), SE: -0.7 (-1.8 to 0.3), 0.54; P=0.19
Green et al, 2011 ⁹³	IG1: Group psychotherapy	HoNOSCA, 6 months, analyzed (IGI=172; CG=180), mean (SD), mean difference (95% CI)
ISRCTN 20496110	(N=183)	IG1: 12.2 (6.3)
	CG: Routine care (N=183)	CG: 12.6 (6.1)
		Difference, mean (95% CI), -0.55 (-1.64 to 0.54), P=0.32
		HoNOSCA, 12 months, analyzed (IGI=168; CG=178), mean (SD), mean difference (95% CI)
		IG1: 10.9 (5.9)
		CG: 11.7 (6.7)
		Difference, mean (95% CI), -0.79 (-1.98 to 0.40), P=0.19

Appendix I Table 14. Suicide Risk Treatment Studies: Functioning Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes
Hazell et al, 2009 ⁹⁵ ACTRN12608000532303	IG1: Group therapy (N=35) CG: Routine care (N=37)	CGAS, 8 weeks, analyzed (IG1=25; CG=25), mean (SD) IG1: 58.54 (8.70) CG: 60.59 (10.69)
		CGAS, 12 months, analyzed (IG1=25; CG=25), mean (SD) IG1: 60.36 (8.48) CG: 60.14 (9.47) F=0.89
		P=0.89 P=0.35 (for group differences from baseline)
		HoNOSCA, 8 weeks, analyzed (IG1=26; CG=29), mean (SD) IG1: 16.77 (7.12) CG: 15.00 (9.28)
		HoNOSCA, 12 months, analyzed (IG1=26; CG=29), mean (SD) IG1: 13.80 (6.83) CG: 15.41(8.75) F=3.77
		P=0.06 (for group differences from baseline)
		SDQ, 8 weeks, analyzed (IG1=33; CG=37), mean (SD) IG1: 17.66 (6.58) CG: 18.89 (7.16)
		SDQ, 12 months, analyzed (IG1=33; CG=37), mean (SD) IG1: 15.14 (7.15) CG: 18.35 (6.26) F=2.60
M: 4 1 2222109	104)/ 11 11 1 1	P=0.11 (for group differences from baseline)
King et al, 2009 ¹⁰⁸ NCT00071617	IG1: Youth-Nominated Support Team (N=223) CG: TAU (N=225)	CAFAS, 3 months, analyzed (IGI=168; CG=174), adjusted mean IG1: 15.20 CG: 15.77 Main effects mixed model, P=0.58
		CAFAS, 12 months, analyzed (IGI=175; CG=171), adjusted mean IG1: 12.43 CG: 12.70
		Main effects mixed model, P=0.70

Appendix I Table 14. Suicide Risk Treatment Studies: Functioning Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes
Mehlum et al, 2014 ¹¹⁵	IG1: DBT (N=39)	CGAS, 71 weeks, mITT(IG1=38; CG=37), mean (SD)
Mehlum et al, 2016 ²⁰¹	CG: Enhanced usual care	IG1: 65.68 (11.81)
Mehlum et al, 2019 ²⁰² Haga et al, 2018 ²⁰³ NCT00675129	(N=38)	CG: 64.22 (14.13) Between-group difference in slope=0.03; P=0.067
NC100075129		CGAS, 3.1 years, mITT(IG1=37; CG=34), mean (SD)
		IG1: 65.0 (11.8)
		CG: 66.1 (11.2)
		Between-group difference in slope= -0.012; P=0.747
		Between-group difference in mean change= -1.1; P=0.678
Ougrin et al, 2013 ¹²¹	IG1: Therapeutic Assessment	CGAS, 3 months, ITT (IG1=35; CG=35), mean (SD)
Ougrin, 2011 ²⁰⁴	(N=35)	IG1: 64.6 (12.9)
ISRCTN 81605131	CG: Assessment as usual	CG: 60.1 (9.9)
	(N=35)	Mean difference: 4.49 (95% CI, -0.98 to 9.96)
Pineda et al, 2013 ¹²⁵	IG1: RAP-P (Family	HoNOSCA, posttreatment, completers (IG1=22; CG=18), mean (SD)
ACTRN12613000668707	Intervention) (N=24)	IG1: 13.45 (5.89)
	CG: Routine care (N=24)	CG: 17.61 (5.20)
		HoNOSCA, 6 months, completers (IG1=22; CG=18), mean (SD)
		IG1: 4.77 (4.45)
		CG: 12.72 (5.29)
		Time x Group interaction (presumably across both timepoints): P=0.01, favoring RAP-P
Wood et al, 2001 ¹⁵⁹	IG1: Developmental Group	HoNOSCA, change from baseline to 7 months (posttreatment), analyzed (IG1=31; CG=31), mean
	Therapy (N=32)	(SD)
	CG: Treatment as usual	IG1: 8.4 (6.4)
	(N=31)	CG: 6.9 (6.1)
		Mean difference (95% CI), 1.5 (-1.7 to 4.7)

Abbreviations: CAFAS=Child and Adolescent Functional Assessment Scale; CG=control group; CGAS=Children's Global Assessment Scale; CI=confidence interval; DBT=dialectical behavior therapy GHQ-12=General Health Questionnaire, 12 questions; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; IG=intervention group; ITT=intent to treat; KQ=key question; mITT=modified intent to treat; PQ-LES=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; RAP-P=Resourceful Adolescent Parent Program; SD=standard deviation; SDQ=Strengths and Difficulties Questionnaire; SE=standard error; TAU=treatment as usual.

Appendix I Table 15. Suicide Risk Treatment Studies: Subgroups (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Other Outcomes/ Subgroups
Diamond et al, 201082	IG1: Attachment-	Adolescents diagnosed with depression
NCT00604097	Based Family	SIQ-Jr, 24 weeks, analyzed (IG1=19; CG=16), total change from baseline (SE)
	Therapy (N=35)	IG1: -4.35 (0.66)
	CG: Enhanced Usual	CG: -2.19 (0.62)
	Care (N=31)	Difference in difference from baseline to followup: 2.16 (SE=0.91), effect size=1.00, in favor of IG1 (t(64=-2.39, p=0.02)
Cottrell et al, 201880	IG1: Family therapy	Moderator analysis for repetition of self-harm leading to hospital attendance
Cottrell et al, 2018 ¹⁹⁹	(N=415)	Age: chi-square=0.4730, P=0.49
Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	CG: TAU (N=417)	Sex: chi-square=1.5219, P=0.2173

Abbreviations: CG=control group; IG=intervention group; KQ=key question; SE=standard error; SIQ-Jr=Suicidal Ideation Questionnaire-Junior; TAU=treatment as usual.

Appendix I Table 16. Suicide Risk Treatment Studies: Harms (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Other Harms
Cottrell et al, 2018 ⁸⁰ Cottrell et al, 2018 ¹⁹⁹ Cottrell et al, 2018 ²⁰⁰ ISRCTN59793150	IG1: Family therapy (N=415) CG: TAU (N=417)	One or more AE, 12 to 18 months followup, ITT (IG1=415; CG=417), N% IG1: 226 (54) CG: 217 (52) One or more accident and emergency/MIU/WIC attendance, 12 to 18 months followup, ITT (IG1=415, CG=417), N% IG1: 258 (62) CG: 253 (61)	One or more SAE, 12 to 18 months followup, ITT (IG1=415; CG=417), N (%) IG1: 156 (38) CG: 141 (34)	Two respondents died between 3 and 4 years postrandomization. Both participants were assigned to the Family Therapy group, neither death was related to self-harm.
Griffiths et al, 201994 NCT02771691	IG1: MBT (N=26) CG: TAU (N=27)	5 AEs among 4 participants (not reported by group); none were considered to be trial related	NR	NR

Abbreviations: AE=adverse event; CG=control group; IG=intervention group; ITT=intent to treat; KQ=key question; MBT=mentalization-based treatment; MIU=minor injury unit; N=number; NR=not reported; SAE=serious adverse event; SIQ JR=Suicidal Ideation Questionnaire-Junior; TAU=treatment as usual; WIC=walk-in center.

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Arendt et al, 2016 ⁶⁵	Other very high HDI Denmark RCT TrygFonden	Recruited from a training and research clinic at a University Department of Psychology and Behavioural Sciences	IG1: Group child+parent in-person CBT (N=56) Description: Manualized group CBT program (Cool Kids) with a focus on teaching youths to recognize their emotions, restructure negative automatic thinking, and gradually confront feared situations. The treatment consisted of 10 2-hour weekly group sessions with 6 to 7 youths and their parents in each group. Duration: 10 weeks	CG: Wait-list (N=53) 3-month wait-list. All participants in the wait- list condition were offered the Cool Kids treatment after the waiting period	Some concerns
Asbrand et al, 2020 ⁶⁷ TU 78/5-2, HE 3342/4-2	Other very high HDI Germany RCT German Research Foundation	Recruited through advertisements in schools and medical facilities and through newspaper articles in 2 midsized German cities	IG1: Group child-focused in-person CBT (N=31) Description: Exposure-based CBT with 12 sessions (100 minutes each, including a 10-minute break) in groups of 5 to 7 children. Intervention components consist of psychoeducation, cognitive restructuring, social skills training, exposure, and relapse prevention. Duration: 12 weeks	CG: WLC (N=36) Wait-list control group receiving therapy about 16 weeks later	Some concerns
Barrett et al, 1996 ⁷⁰	Other very high HDI Australia RCT The National Health and Medical Research Council of Australia, The Myer Foundation of Australia	Recruited from referrals from community centers, schools, mental health professionals, and medical practitioners, or parents referred them after media releases	IG1: CBT (N=28) Description: Seen on a weekly basis for 60 to 80 minutes using Coping Koala Workbook, which included recognizing anxious feelings and somatic reactions to anxiety, cognitive restructuring in anxiety-provoking situations, coping self-talk, exposure to feared stimuli, evaluating performance, and administering self-reinforcement as appropriate. The first 4 sessions were training sessions in which anxiety management procedures were introduced, role-played by the therapist, and practiced by each child. For the remaining 8 sessions, each child practiced the anxiety coping skills by using in vivo exposure to feared situations, starting with the low-stress situations and gradually increasing to high-stress situations. IG2: CBT + Family Intervention (N=25)		

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Barrett et al, 1996 ⁷⁰ (continued)			Description: Same as IG1 plus parallel program called Family Anxiety Management (FAM) consisting of child/parent therapy sessions after each CBT session; therapy emphasized methods for empowering parents and children focusing on 1) how to reward courageous behavior and extinguish excessive anxiety, 2) teaching parents to deal with their own upsets and awareness of their own anxiety responses, and 3) brief training in communication and problem-solving.	CG: Wait-list (N=26) 12-week waiting period, participants still meeting criteria at followup were offered the family intervention treatment	Some concerns
Dirmohar at al	U.S.	Described through	Duration: 12 weeks	CC: Placeba (N. 27)	Some
Birmaher et al, 2003 ⁷³	RCT NIMH. Eli Lily	Recruited through advertisements and from an outpatient	IG1: Fluoxetine (N=37) Description: Fluoxetine (10 mg/day, after first week increasing to 20 mg/day if tolerated).	CG: Placebo (N=37) Placebo	concerns
	provided fluoxetine and placebo	clinic	Duration: 12 weeks		
Black et al, 1994 ⁷⁴	U.S. RCT NR	Recruited through announcements to school counselors in all elementary schools in Maryland, Virginia, and the District of Columbia	IG1: Fluoxetine (N=6) Description: Fluoxetine 0.2 mg/kg for 1 week, then 0.4 mg/kg for 1 week, then 0.6 mg/kg for 10 weeks. Duration: 12 weeks	CG: Placebo (N=9) Placebo syrup for 12 weeks	Some concerns
Cobham et al, 2017 ⁷⁷ ACTRN12615000 514505	Other very high HDI Australia RCT Triple P is owned and distributed by the University of Queensland	Recruited through media and schools	IG1: Group parent-only in-person CBT (N=33) Description: Six 90-minute parent-only group-based CBT sessions focused on psychoeducation about parents role in the maintenance of anxiety, promoting emotional resilience, understanding the role of thoughts in anxiety and how to challenge them, avoidance and exposure, comment parental responses to children's anxiety, promoting coping, and maintaining gains. Concepts are translated into homework tasks and parents are encouraged to apply these principles and instruct children in the content they are learning. Duration: 6 weeks	CG: Wait-list control (N=30) Families in the wait-list condition were reassessed following the 6-week wait and then received the intervention	Low/ some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Cornacchio et al, 2019 ⁷⁹ NA	U.S. RCT National Institute of Health; American Psychological Association Division 53 Society for Clinical Child and Adolescent Psychology	Selective mutism specialty treatment center in metropolitan region in the southeast U.S. Families were typically referred by other programs or professionals in the field, their school, or by reading about the program online or in the news.	IG1: Group child+parent in-person CBT (N=14) Description: 5 consecutive days of 6- to 8-hour treatment; intensive group CBT program centered around graduated exposure to verbal communication that relies on the early child format of Parent Child Interaction Therapy. Each group consisted of approximately 10 children of similar age with a ratio of 1 staff counselor to 1 child. Child group treatment sessions occurred Monday to Friday and focused on verbalizations and social strategies. Staff relied on Child Directed Interaction and Verbal Directed Interaction skills and employed reinforcement, prompting, shaping, stimulus fading, graduated exposure, social skills training, cognitive strategies, relaxation training, and modeling strategies. Parent group training sessions occurred Monday to Thursday for 2 hours each session and focused on psychoeducation about selective mutism, interaction strategies for optimizing positive relationships, and eliciting verbal behavior. Therapists coached parents in vivo with their child in the implementation of these skills. Duration: 5 days	CG: Wait-list control (N=15) Wait-list control, following a 4-week period group CBT was offered to wait-list families.	Some concerns
Donovan et al, 2014 ⁸³ ACTRN12612000 139875	Other very high HDI Australia RCT Australian Rotary Health	Recruited through media releases, general practitioners, childcare, and school newsletters throughout Australia.	IG1: Individual parent-focused internet CBT (N=23) Description: Online individual parent-focused CBT; six 1- hour session and 2 boosters, one telephone call and weekly emails from online therapist. Content of sessions: psychoeducation about anxiety, strategies for managing anxious child behavior, relaxation, coping self-talk, exposure, and social problem-solving. Duration: 6 sessions (8 weeks)	CG: Wait-list (N=29) Wait-list	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Ginsburg et al, 2020 ⁹²	U.S. Other Institute of Education Sciences, U.S. Department of Education	Recruited via referrals from clinicians, school personnel, parents, or self-referrals.	IG1: Individual child-focused in-person CBT (N=148) Description: Modular CBT consisted of 7 core modules: psychoeducation, exposure, rewards, cognitive restructuring, problem-solving, somatic/relaxation skills, and relapse prevention; an optional parental psychoeducation module was available. Treatments were administered individually over 12 sessions, with each session lasting 30 to 40 minutes. Duration: 12 weeks	CG: TAU (N=68) TAU reflected the therapeutic strategies that clinicians would typically provide to students with anxiety (e.g., supportive therapy).	Some concerns
Hirshfeld-Becker et al, 2010 ⁹⁸	U.S. RCT NIH, Mass General Hospital Brandon Shedd Fund	Recruited from an outpatient child psychiatry clinic at a general hospital; through print advertisements in local newspapers and parent magazines, email advertisements to hospital employees, and posters at local pediatric practices	IG1: Individual child+parent in-person CBT (N=34) Description: Being Brave manualized CBT intervention included up to 20 sessions over 6 months. First 6 sessions and session 20 were parent only, with a flexible number of parent-child sessions ranging from 8 to 13 depending on number needed to complete exposure exercises to several feared situations. Content of sessions 1 to 3 includes learning about anger management and modeling coping skills; content of sessions 4 to 6 includes coaching the child in anxiety management; content of parent-child sessions 7 to 19 involves child anxiety management such as coping plans and graduated exposure. Parent-only session 20 covers maintaining gains. Duration: 6 months	CG: Wait-list control (N=30) Wait-list control, participants offered treatment after 6 months.	Some concerns
Holmes et al, 2014 ⁹⁹ ACTRN12612000 061831	Other very high HDI Australia RCT Griffith University Behavioural Basis of Health	Referred by parents, teachers, guidance officer networks, school newsletters, child and youth mental health services, and social media forums.	IG1: Group child-focused in-person CBT (N=20) Description: 10 weekly group-based 90-minute sessions followed by two booster sessions, conducted 1 and 3 months after the completion of the initial program. Parents concurrently complete seven 90-minute sessions as well as the two booster sessions. The group CBT program termed "No Worries!" utilizes the A-B-C model and provides psychoeducation about anxiety and worry and relaxation training. The majority of the program targets children's intolerance of uncertainty, positive and negative beliefs about worry, negative problem orientation, cognitive avoidance, sleep issues associated with worry, and perfectionism. Duration: 10 weeks	CG: Wait-list control (N=22) After 12 weeks participants in the wait-list condition were reassessed and offered the treatment program.	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Ishikawa et al, 2019 ¹⁰³	Other very high HDI Japan RCT Japan Society for the Promotion of Science	Recruited using advertisements displayed at schools, public mental health clinics, and in newspapers and websites.	IG1: Individual child+parent in-person CBT (N=26) Description: Japanese Anxiety Children/Adolescents Cognitive Behavior Therapy program (JACA-CBT) adapted over 4 phases to allow increased suitability for Japanese children. CBT was provided once per week for 8 sessions and homework was assigned between the sessions. Booster sessions mainly focused on the family's implementation of the in vivo exposures in their daily life and were provided once per 1 to 3 months and until 6 months after the completion of therapy depending on the needs of each participant. Duration: 8 weeks, with up to 3 subsequent booster sessions until 6 months after completion of therapy	CG: Wait-list (N=25) Wait-list participants visited the clinic 2 months after the pretreatment assessment for a second assessment session (mean [SD] 70.0 days [11.0]), after which they started to participate in the CBT program	Some concerns
Lau et al, 2010 ¹¹⁰ NR	Other very high HDI Hong Kong, China RCT NR	Referred by physicians or psychologists to the Child Assessment Service for one or more of the following concerns: learning, behavior, moodrelated, anxiety, and other developmental problems.	IG1: Group child+parent in-person CBT (N=26) Description: Nine 2-hour weekly sessions (8 sessions followed by a 2-week break and 1 final session) of the Coping Cat CBT group-treatment program. Sessions included the use of puppet play, competitive games, worksheets, and question-and-answer format to cover core CBT elements, including recognizing anxiety symptoms, combating cognitive bias with cognitive restructuring, practicing gradual exposure to anxiety-provoking stimuli, and evaluating and rewarding one's coping. Parents were invited to observe treatment to learn coaching techniques and asked to provide realworld practice opportunities for their children during the week. Children were asked to complete worksheets.	CG: Wait-list control (N=25) After completing the baseline and second assessment, children in the wait-list condition received the 9-session treatment followed by a posttreatment assessment.	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Lyneham et al, 2006 ¹¹² NR	Other very high HDI Australia RCT Financial Markets Foundation for Children	Self-referrals to clinic in response to recommendations from counselor, teacher, local community health services, or after seeing advertisement in school newsletter.	IG1: Parent-guided CBT supported by telephone (N=28) Description: Parents received a self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion that broke the program into 12 weekly modules. A child's workbook was provided that described each anxiety management skill in child- friendly language and included example applications as well as practice exercises. Each week parents were directed to read sections of the self-help book and complete activities to apply what they learned, and to complete certain activities with their child. Daily practice tasks were provided to reinforce weekly activities. Parents received 9 telephone calls. Phone calls occurred weekly for the first 6 weeks and then biweekly for the last 6 weeks. IG2: Parent-guided CBT supported by email (N=21) Description: Parents received a self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion that broke the program into 12 weekly modules. A child's workbook was provided that described each anxiety management skill in child- friendly language and included example applications as well as practice exercises. Each week parents were directed to read sections of the self-help book and complete activities to apply what they learned, and to complete certain activities with their child. Daily practice tasks were provided to reinforce weekly activities. Parents received 9 emails—emails occurred weekly for the first 6 weeks and then biweekly for the last 6 weeks.	CG: Wait-list (N=22) Families allocated to the wait-list condition were sent a confirmation letter indicating when their second assessment would take place. Families were given the choice of completing the treatment program by phone, email, or on their own.	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Lyneham et al, 2006 ¹¹² NR (continued)			IG3: Parent-guided CBT with as needed support (N=29) Description: Parents received a self-help book (Helping Your Anxious Child: A Step by Step Guide for Parents) and a workbook companion that broke the program into 12 weekly modules. A child's workbook was provided that described each anxiety management skill in child-friendly language and included example applications as well as practice exercises. Each week parents were directed to read sections of the self-help book and complete activities to apply what they learned, and to complete certain activities with their child. Daily practice tasks were provided to reinforce weekly activities. Parents were given the option to contact their therapist by phone or email as many times as they needed during the 12-week period. All contact with therapist was parent initiated.		
Ost et al, 2015 ¹²⁰	Other very high HDI Sweden RCT Swedish Council for Working Life and Social Research; Swedish Research Council	Recruited through referrals from the child psychiatric services and school health services in Stockholm County, Sweden	IG1: Individual+group child (N=16) Description: 12 individual weekly sessions plus 12 social skills group weekly sessions. Individual sessions focused on exposure to situations causing anxiety. Group social skills training on topics such as introducing oneself, starting a conversation, making phone calls, and assertiveness training. Therapist introduced importance of topic, demonstrated the skill, and then youth practiced skill.	CG: Wait-list (N=23) Wait-list	Some concerns
			IG2: Child+parent in-person CBT (N=16) Child Treatment same as IG1 Description: Parent training consisted of 8 sessions of 90 minutes run concurrently with child's treatment. First 4 sessions were weekly then last 4 were biweekly. Sessions designed to teach parents about SocAD and how they can help their children in general and with practicing skills learned in group sessions, not reinforcing anxious behavior, modeling socially proactive behavior, and encouraging youth to participate in social activities. Duration: 12 weeks		

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Perrin et al, 2019 ¹²² ISRCTN50951795	Other very high HDI United Kingdom RCT National Institute of Health Research, Guy's & St Thomas' Charity, NIHR Biomedical Research Centre at the South London, Maudsley NHS Foundation Trust and King's College London	Recruited from referrals to child and adolescent mental health services and a specialist child anxiety disorders clinic in the United Kingdom	IG1: Individual child+parent in-person+internet CBT (N=20) Description: 10 sessions of individual, GAD-specific CBT. Sessions proceeded sequentially through 6 modules: worry awareness training, planned exposure to uncertainty; modification of dysfunctional beliefs about worry; modified problem-solving training; imaginal exposure to unpleasant images or worries; and relapse prevention. During each session the therapist would elicit a concrete episode of worry from the past week that was tied to behavioral experiments and imaginal exposures. Homework tasks were provided and included: pausing several times a day to reflect upon, write down, and distinguish between worries about current problems vs. hypothetical situations; plan daily confrontations with situations that involve uncertainty and normally trigger worries; reducing requests for reassurance from others; practicing behavioral experiments to test dysfunctional beliefs; engaging in self-guided exposures to the context of worries to test tolerance of uncertainty and distress.	CG: Wait-list control (N=20) Wait-listed participants were provided information about the prevalence of worry and GAD, 10 copies of the self-report measures of worry (PSWQ-C) and pre-paid envelopes. Wait-list participants were asked to complete and return the PSWQ-C at the end of each week for 10 weeks.	Low/ Some Concerns
Pine et al, 2001 ¹²⁴ Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵	U.S. RCT NIMH, Research Foundation for Mental Hygiene; National Center for Research Resources - NIH General Clinical Research Center	Recruited from clinics at 5 academic medical centers.	IG1: Fluvoxamine (N=63) Description: Fluvoxamine 50 mg daily to start, then increased 50 mg per week to a maximum of 300 mg per day in adolescents and 250 mg per day in children younger than 12 years of age. Duration: 8 weeks	CG: Placebo (N=65) Placebo	Some concerns

Author, Year	Country Study Design				
Registry Number	Funding	Setting	Intervention(s)	Comparator	Quality
Rudy et al, 2017 ¹²⁹ NCT02051192	U.S. RCT NR	Children who presented to a university-based clinic for inclusion in an RCT evaluating the effectiveness of a behaviorally-based, parent-led treatment approach	IG1: Individual parent-led in-person CBT, (N=12) Description: Ten 60- to 90-minute sessions, twice weekly over 5 weeks. The first session focused on psychoeducation and treatment preparation and only included parents. The subsequent 9 sessions consisted of exposure therapy using participant modeling and reinforced practice of behavioral techniques for alleviating anxiety. Sessions 2 to 5 were therapist-led while parents observed. Sessions 6 to 10 were parent-led with the therapist serving as a coach and providing in the moment feedback. Families were encouraged to complete daily home exercises that aligned with skills practiced in session. Duration: 5 weeks	CG: TAU (N=10) Patients randomized to the TAU condition were instructed to continue receiving any prior interventions as recommended by their providers (e.g., psychotherapy, social skills training, behavioral interventions, family participation in family therapy or a parenting class, or pharmacoligcal interventions). Treatment changes were not prohibited but monitored.	Some concerns
Rynn et al, 2001 ¹³⁰	U.S. RCT University of Pennsylvania and NIMH	Referrals by psychiatrists and pediatricians	IG1: Sertraline (N=11) Description: Sertaline once daily, 25 mg for the first week and 50 mg for weeks 2 to 9. Duration: 9 weeks	CG: Placebo (N=11) Placebo	Some concerns
Salzer et al, 2018 ^{42,} ISRCTN 22752528	Other very high HDI Germany RCT German Federal Ministry of Education and Research	Recruited from outpatient clinics at universities in 4 German cities via mass media announcements or referral by private practice therapists and physicians.	IG1: Individual child-focused in-person CBT (N=34) Description: 25 individual 50-minute treatment sessions as well as up to 5 preparatory sessions. CBT focused on reducing self-focused attentional and safety behaviors through use of role plays, attentional training, and behavioral experiments. Duration: 31 weeks	CG: Wait-list control (N=39) Wait-list; after a waiting period of 4 months, patients were offered an active treatment, either CBT or psychodynamic therapy	Some concerns

NR Spain RCT Ministry of Science and Education; Seneca Foundation Seneca Foundation Region of Murcia completed the Inventory of Anxiety and Social Phobia (SPAI-C) and the revised Social Anxiety Scale for Children (SASC) MR Spain RCT Ministry of Science and Education; Seneca Foundation Seneca Foundation Seneca Foundation Description: 12 weekly group sessions, each lasting 90 minutes, referred to as Intervencion en Adolescentes con Fobia Social (IAFS). Group sessions are designed to expose participants to feared social situations and consist of four components: 1) education (information on treatment is provided, explanatory model of social phobia is presented, objectives are planned); 2) training in social skills (starting and holding conversations, assertiveness, making and maintaining friends, public speaking); 3) exposure (exposure to situations listed above such as starting and maintaining conversations with audiovisual, video, and group feedback provided); and 4) cognitive restructuring (a combination of Beck's cognitive therapy and Ellis's rational emotional therapy are used). IG2: Group CBT without cognitive restructuring (N=29) Description: 12 weekly group sessions, each lasting 90	Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
expose participants to feared social situations and consist of three components: 1) education (information on treatment is provided, explanatory model of social phobia is presented, objectives are planned); 2) training in social skills (starting and holding conversations, assertiveness, making and maintaining friends, public speaking); and 3) exposure (exposure to situations listed above such as starting and maintaining conversations with audiovisual, video, and group feedback provided). Duration: 12 weeks	et al, 2009 ¹³¹	HDI Spain RCT Ministry of Science and Education;	occurred in two phases. In phase 1, 2,931 students in 17 public and semi- public educational centers in the Region of Murcia completed the Inventory of Anxiety and Social Phobia (SPAI-C) and the revised Social Anxiety Scale for	(N=28) Description: 12 weekly group sessions, each lasting 90 minutes, referred to as Intervencion en Adolescentes con Fobia Social (IAFS). Group sessions are designed to expose participants to feared social situations and consist of four components: 1) education (information on treatment is provided, explanatory model of social phobia is presented, objectives are planned); 2) training in social skills (starting and holding conversations, assertiveness, making and maintaining friends, public speaking); 3) exposure (exposure to situations listed above such as starting and maintaining conversations with audiovisual, video, and group feedback provided); and 4) cognitive restructuring (a combination of Beck's cognitive therapy and Ellis's rational emotional therapy are used). IG2: Group CBT without cognitive restructuring (N=29) Description: 12 weekly group sessions, each lasting 90 minutes, termed IAFS. Group sessions are designed to expose participants to feared social situations and consist of three components: 1) education (information on treatment is provided, explanatory model of social phobia is presented, objectives are planned); 2) training in social skills (starting and holding conversations, assertiveness, making and maintaining friends, public speaking); and 3) exposure (exposure to situations listed above such as starting and maintaining conversations with audiovisual, video, and group feedback provided).	(N=25) Participants in the wait-list control began receiving treatment after the first followup	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Shortt et al, 2001 ¹³⁴	Other very high HDI Austrailia RCT NR	Recruited from child mental health centers, school guidance officers, and parents who responded to advertisements	IG1: Group child+parent in-person CBT (N=54) Description: 10 weekly Family Based Cognitive Behavioral therapy sessions termed "FRIENDS" with 5 to 13 children and 1 or more parents per family. Sessions included a 10-minute joint parent-child meeting to provide outline of session and homework; a 50- to 60- minute youth session; a 5-minute session after youth session with parents to review strategies to practice, and a 30- to 40-minute parent session. Booster sessions were given at 1 and 3 months following the end of treatment. Program adapted from Coping Koala Workbook, which was adapted from the Coping Cat Workbook.	CG: Wait-list (N=17) Wait-list	Some concerns
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	Other very high HDI Denmark RCT Trygfonden and Edith and Godtfred Kirk Christiansens Fund	Families self- referred after reading announcements on website or learning about study from community health services	Duration: 10 weeks IG1: Individual child-focused internet CBT (N=35) Description: Based on Cool Kids and Chilled anxiety management program; 8 online sessions of CBT of approximately 30 minutes each plus homework practice that focuses on psychoeducation, cognitive restructuring, and graded exposure. Content includes goal setting, realistic thinking, problem-solving, and assertiveness and is presented using a variety of formats such as text, audio, illustration, cartoons, worksheets, and video vignettes. Youth rate the interference of anxiety in their lives weekly. Youth received a 20-minute weekly call from their therapist. Parents were given a resource describing their role in treatment and the treatment's core strategies; parents were encouraged to provide support and encouragement to their youth. Therapists called parents within first 2 weeks to answer questions.	CG: Wait list control group (N=35) Wait-list, participants asked not to engage in other forms of treatment or make changes to their use of psychiatric medication. Participants offered treatment after 14 weeks.	Low/ Some Concerns
Strawn et al, 2015 ¹⁴² NCT01226511	Multicountry United States, Mexico, and South Africa RCT Eli Lilly and Company	NR	IG1: Duloxetine (N=135) Description: Flexibly dosed duloxetine (30 to 120 mg once daily). Duration: 10 weeks	CG: Placebo (N=137) Placebo	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Strawn et al, 2020 ¹⁴³ NCT02818751	U.S. RCT National Institute of Mental Health, NIH	Recruited from a single academic site	IG1: Escitalopram (N=26) Description: Escitalopram (forced titration to 15 mg/d, then flexible titration to 20 mg/d). Duration: 8 weeks	CG: Placebo (N=25) Placebo	Low/ Some Concerns
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	Other very high HDI United Kingdom RCT Medical Research Council	Recruited from referrals made to community mental health services anxiety clinic from primary and secondary care	IG1: Parent-delivered brief CBT (N=61) Description: Parents were given a self-help book and received bimonthly therapist contact over 8 weeks, involving two 1-hour in-person sessions and two 20-minute phone sessions (2 hours and 40 minutes of therapist guidance). Sessions covered causal and maintaining factors of anxiety; how to identify and challenge child anxious thoughts; parental responses to child anxiety and graduated exposure; and problemsolving. Parents completed homework tasks between sessions independently and with their child. IG2: Parent-delivered full CBT (N=64) Description: Parents were given a self-help book and received weekly therapist contact over 8 weeks, involving four 1-hour in person sessions and four 20-minute phone sessions (5 hours and 20 minutes of therapist guidance). Sessions covered causal and maintaining factors of anxiety; how to identify and challenge child anxious thoughts; cognitive restructuring; graduated exposure; and problem-solving. Parents completed homework tasks between sessions independently and with their child. Duration: 8 weeks	CG: Wait-list control (N=69) Wait-list families were asked to refrain from starting any other intervention for children's anxiety for 12 weeks. Following posttest assessments at 12 weeks, wait-list families who still required treatment were offered guided parent- delivered CBT	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Villabo et al, 2018 ¹⁵⁰ NR	Other very high HDI Norway RCT NR	Recruited from child and adolescent mental health service clinics in southeastern Norway	IG1: Individual CBT (N=55) Description: Based on Norwegian translation of the CopingCat manual. 14 sessions (12 child sessions and 2 parent sessions) focused on anxiety management skills and tailored behavioral exposures to anxiety-provoking situations. IG2: Group CBT (N=55) Description: 14 sessions (12 child and 2 parent sessions) delivered in group format over 12 weeks consisting of CBT using the Coping Cat manual. Each child received training in anxiety management skills and behavioral exposure to anxiety provoking situations. Met individually with 1 of the 2 group therapists for the first 3 sessions, then sessions 4 to 14 in a group with 3 to 5 participants.	CG: Wait-list (N=55) Following the 12 week wait-list period participants were re- randomized to one of of the two treatment formats.	Some
Waite et al, 2019 ¹⁵² ISRCTN79652741	Other very high HDI United Kingdom RCT National Institute for Health Research (NIHR) Clinical Research Network, Medical Research Council (MRC) Clinical Research Training Fellowship	Recruitment from referrals to a child and adolescent mental health services clinic	IG1: Individual child+parent internet CBT (N=30) Description: A 10-week intervention with 10 treatment sessions and 2 booster sessions of internet-delivered CBT anxiety management strategies (psychoeducation, relaxation training, recognition of the physiological symptoms of anxiety, cognitive strategies of coping, self-talk and cognitive restructuring, graded exposure, and problem-solving) with accompanying parent sessions for half the group and no parent sessions for the other half. Duration: 10 weeks	CG: Wait-list control (N=30) Wait-list control for 10 weeks	Some concerns

Author, Year Registry Number	Country Study Design Funding	Settina	Intervention(s)	Comparator	Quality
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	U.S. RCT NIMH; Pfizer provided sertraline and matching placebo free of charge	Participants were recruited (not reported how) by investigators at medical centers in 6 cities (Durham, NC; New York, NY; Baltimore, MD; Philadelphia, PA, Los Angeles, CA; Pittsburgh, PA).	IG1: Individual child-focused in-person CBT (N=139) Description: 60-minute sessions of 12 individual CBT using Coping Cat program adapted for the child's age and length of the study and 2 parent-only sessions. Therapy included training in anxiety management skills and behavioral exposure to anxiety-provoking situations. Parents attended weekly check-ins and 2 parent-only sessions. IG2: Sertraline (N=133) Description: Sertraline, beginning with 25 mg/day, up to 200 mg/day by 8th week, for 12 weeks. IG3: CBT + Sertraline (N=140) Description: Sertraline, beginning with 25 mg/day, up to 200 mg/day by 8th week, for 12 weeks. Plus 12 sessions of 60-minute individual Coping Cat CBT, including training in anxiety management and exposure to anxiety- provoking situations as well as 2 parent-only sessions. IG3: CBT + Sertraline (N=140) Description: Sertraline, beginning with 25 mg/day, up to 200 mg/day by 8th week, for 12 weeks. Plus 12 sessions of 60-minute individual Coping Cat CBT, including training in anxiety management and exposure to anxiety- provoking situations as well as 2 parent-only sessions. Duration: 12 weeks	CG: Placebo (N=76) Pill placebo	Some concerns
111 111 120		l	Duration, 12 weeks	7.6	

Abbreviations: A-B-C= antecedents, behavior, consequences; CBT=cognitive behavioral therapy; CG=control group; FAM=Family Anxiety Management; GAD=generalized anxiety disorder; HDI=Human Development Index; IAFS=Intervencion en Adolescentes con Fobia Social; IG=intervention group; JACA-CBT=Japanese Anxiety Children/Adolescents Cognitive Behavior Therapy; KQ=key question; MRC=Medical Research Council; NA=not available; NHS=National Health Service; NIH=National Institutes of Health; NIHR=National Institute for Health Research; NIMH=National Institute of Mental Health; NR=not reported; PSWQ-C=Penn State Worry Questionnaire for Children; RCT=randomized, controlled trial; SASC=Social Anxiety Scale for Children; SD=standard deviation; SocAD=social anxiety disorder; SPAI-C=Social Phobia and Anxiety Inventory for Children; TAU=treatment as usual; U.S.=United States; WL=wait-list; WLC=wait-list; WLC=wait

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Arendt et al, 2016 ⁶⁵	Mean age (SD): 11.8 (2.7) N (%) Female: 62 (57) Race/Ethnicity: NR	An anxiety disorder as the primary diagnosis	Psychosis, untreated ADHD, intellectual disability and severe behavior disorders.	Primary diagnosis SepAD: 33.0% GAD: 23.9% SocAD: 15.6% Specific phobia: 14.7% OCD: 7.3% Panic disorder with agoraphobia: 0.9% Agoraphobia without panic disorder: 4.6% Comorbid diagnoses Anxiety disorders: 70.6% No comorbidity: 15.6% Externalizing disorders: 11.9% Mood disorder: 9.2% Other: 6.4%
Asbrand et al, 2020 ⁶⁷ TU 78/5-2, HE 3342/4-2	Mean age (SD): IG1: 11.5 (1.35) CG: 11.2 (1.33) N (%) Female: IG1: 16 (51.6) CG: 24 (67.6) Race/Ethnicity: NR	Ages 9 to 13 years with a primary diagnosis of SocAD	Health problems (e.g., asthma, cardiac arrhythmia) and medication (e.g., methylphenidate) that could have interfered with psychophysiological assessment.	SocAD: 100% Comorbid diagnoses: IG1: 41.9% CG: 45.9%
Barrett et al, 1996 ⁷⁰	Mean age (SD): IG1: 9.7 (2.5) IG2: 10.1 (1.9) CG: 8.2 (1.9) N (%) Female: 34 (43) Race/Ethnicity: NR	Has a principal diagnosis of overanxiety disorder, separation anxiety disorder, or social phobia.	Intellectual or physical disabilities, currently taking antianxiety or depression medication, or parents were involved in acute marital breakdown.	Principal diagnosis Overanxiety disorder: 38% SepAD: 38% Social phobia: 24% Other comorbid conditions Depression: 6% Simple phobia: 22% Oppositional disorder: 2%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Birmaher et al, 2003 ⁷³	Mean age (SD): 11.8 (2.8) N (%) Female: 40 (54) Race/Ethnicity: 71 (96) White 1 (1) Asian 2 (3) Biracial	Ages 7 to 17 years with DSM-IV GAD, SAD, and/or SP who had significant impairment in functioning	Current MDD; lifetime bipolar, OCD, PTSD, eating disorder, substance abuse, PDD, and mental retardation; significant medical and neurological illness; prior trials with SSRIs; current medications that may affect the central nervous system; or pregnancy.	Primary target conditions (participants could have more than 1 condition) SepAD: 47% GAD: 64% SocAD: 55% Other comorbid conditions (past or current, participants could have more than 1 condition) Past or current simple phobia: 24% Past MDD: 4% Past or current dysthymia: 4% Past of current ADHD: 5% Past or current ODD: 4%
Black et al, 1994 ⁷⁴	Mean age (SD): 8.5 (NR) N (%) Female: 9 (60) Race/Ethnicity: NR	Ages 6 to 16 years meeting DSM-III criteria for selective mutism	Mental retardation, major medical illness, being treated with medication, mutism symptoms were improving rapidly, less than 14 weeks left in school term, or parents did not speak English.	Primary condition Selective mutism: 100% Comorbid conditions SocAD and/or avoidant disorder: 100% Simple phobia: 33% SepAD: 13% Overanxious disorder: 13% ODD: 13% OCD: 7%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Cobham et al, 2017 ⁷⁷ ACTRN12615000514 505	Mean age (SD): 9.3 (2.0) N (%) Female: IG1: 19 (59) CG:11 (38) Race/Ethnicity: IG1: White: 28 (88) CG: White: 27 (93)	Ages 7 to 14 years meeting diagnostic criteria for a primary DSM-IV anxiety diagnosis and whose parents were able to attend treatment; participants with secondary non-anxiety diagnoses were not excluded	Ongoing treatment including psychological or medication for the child's anxiety.	IG1 Primary/target condition % GAD: 38% SocAD: 13% SepAD: 25% Specific phobia: 19% OCD: 3% Other comorbid conditions % ADHD: 13% ODD: 9% Dysthymia: 3% MDD: 3% Depression NOS: 3% CG Primary/target condition % GAD: 38% SocAD: 41% SepAD: 10% Specific phobia: 10% OCD: 0 Other comorbid conditions % ADHD: 14% ODD: 3% Dysthymia: 3% MDD: 3% Dysthymia: 3% MDD: 3% Depression NOS: 0

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Cornacchio et al, 2019 ⁷⁹ NA	Mean age (SD): 6.6 (1.3) N (%) Female: 22 (76) Race/Ethnicity: White: 24 (83) Black: 2 (7) Asian: 2 (7) Other: 1 (3) Hispanic/Latino: 10 (35)	Ages 5 to 9 years who met DSM-5 criteria for selective mutism. Children with comorbid anxiety disorders, taking stable doses of psychotropic medication (no starting/stopping, dose changes 6 weeks prior to baseline through posttreatment assessment) were included (17% of sample reported taking stable does of psychotropic medication). Required to cease non-study psychotherapeutic activities before baseline assessment through posttreatment assessment.	Presence of comorbid mental health condition more impairing than selective mutism, or nonverbal with both parents.	Primary condition % Selective mutism: 100% Other comorbid conditions % SocAD: 72% SepAD: 28% GAD: 24% Specific phobia: 10% OCD: 7% ADHD: 7%
Donovan et al, 2014 ⁸³ ACTRN12612000139 875	Mean age (SD): 4.1 (0.76) N (%) Female: 28 (54) Race/Ethnicity: NR	Ages 3 to 6 years, primary diagnosis of SocAD, SepAd, GAD, or specific phobia using parent version of Anxiety Disorders Interview Schedule-Child Version	PDD or already receiving psychological treatment.	Primary/target condition SocAD: 56% SepAD: 25% GAD: 2% Specific phobia: 12% Selective mutism: 6% Mean (SD) number of anxiety diagnoses: 2.02 (1.02)
Ginsburg et al, 2020 ⁹²	Mean age (SD): 10.9 (3.3) N (%) Female: 105 (48.6) Race/Ethnicity: Non-Hispanic White: 138 (63.9) Other: 62 (28.7)	Ages 6 to 18 years meeting DSM-IV criteria for a primary anxiety disorder (disorder with the highest CSR). Participants could be on stable doses of medication for a psychiatric disorder.	Medical or psychiatric condition contraindicating study treatment, needing immediate or alternative treatment, receiving psychosocial treatment for anxiety, or in the custody of state social services.	Primary diagnosis % SepAD: 13% SocAD: 22% GAD: 62% Specific phobia: 1% Not otherwise specified: 2% % with comorbid diagnosis SepAD: 10% SocAD: 23% GAD: 17%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Hirshfeld-Becker et al, 2010 ⁹⁸	Mean age (SD): 5.4 (1.0) N (%) Female: 34 (53) Race/Ethnicity: White: 41 (80) Latino: 2 (3) Asian: 5 (8) Biracial/unknown: 6 (9)	Ages 4 to 7 years with a current DSM-IV anxiety diagnosis.	Parental active psychosis, suicidality, or substance abuse; child mental retardation; current psychiatric treatment or past CBT; consensus of two senior clinicians that child was too uncooperative or distractible or too severely symptomatic to wait 6 months to receive treatment.	77% had more than 1 anxiety disorder GAD: 44% SocAD: 67% SepAD: 44% Agoraphobia: 36% Specific phobia: 48%
Holmes et al, 2014 ⁹⁹ ACTRN12612000061 831	Mean age (SD): 9.6 (1.4) N (%) Female: 28 (67) Race/Ethnicity: NR	Ages 7 to 12 years meeting DSM-IV criteria for a primary diagnosis of GAD with an ADIS-C/P CSR of at least 4 and a minimum reading level of 7 years.	Diagnosis of behavioral problems more impairing than anxiety, PDD, intellectual handicap, learning disability, or presence of substance abuse, self-harm, or suicidal ideation, currently receiving psychological assistance or medical treatment.	Primary condition: GAD: 100% Other comorbid conditions: SepAD: 64% Specific phobia: 88% SocAD: 76% Dysthymia: 7% MDD: 5% ADHD: 21% ODD: 14%
Ishikawa et al, 2019 ¹⁰³	Mean age (SD): 10.9 (2.0) N (%) Female: 29 (57) Race/Ethnicity: Asian (Japanese): 51 (100)	Ages 7 to 15 years with an anxiety disorder as determined through the ADIS for DSM-IV, agree to attend treatment with their parents, and discontinue other forms of therapy during the study.	PTSD, disruptive behavioral disorders, substance abuse, mental retardation, pervasive developmental disorder, or a psychotic disorder.	Principle diagnosis SepAD: 0% SocAD: 61% GAD: 14% Specific phobia: 18% Depression: 2% Dysthymia: 6% No. of comorbid disorders 1: 25% 2: 29% 3 or more: 45%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Lau et al, 2010 ¹¹⁰ NR	Mean age (SD): 8 years 7 months (14 months) N (%) Female: 21 (47) Race/Ethnicity: NR	Ages 6 to 11 years with diagnosed anxiety disorder or with subclinical symptoms of anxiety	Presence of only specific phobia diagnosis or severe hyperactivity symptoms.	Primary condition % GAD: 38% SepAD: 24% SocAD: 51% Subclinical symptoms of anxiety disorders: 18% Other comorbid conditions % ADHD: 14% Developmental coordination disorder: 7% Selective mutism: 7%
Lyneham et al, 2006 ¹¹² NR	Mean age (SD): 9.4 (2.0) N (%) Female: 49 (49) Race/Ethnicity: Australian: 90 (90) European: 6 (6) Asian: 1 (1) Other: 3 (3)	Ages 6 to 12 years, living a minimum of 1-hour drive from a specialist anxiety service, and continued medications allowed if on stable doses for 1 month prior to entry	NR	Primary diagnosis % GAD: 40% SepAD: 22% SocAD: 21% OCD: 9% Specific phobia: 7% Panic disorder: 1% Comorbid conditions % Secondary anxiety diagnosis: 86% ODD: 8% Mood disorder: 6% ADHD: 3% Asperger's: 2% Tourette's disorder: 1%
Ost et al, 2015 ¹²⁰	Mean age (SD): 11.6 (2.0) N (%) Female: 34 (62) Race/Ethnicity: NR	Ages 8 to 14 years meeting DSM-IV criteria for SocAD as the primary diagnosis; severity had to be at least 4 on the clinician severity scale of the ADIS-C/P; duration of the phobia ≥1 year; motivated for treatment; and parents and participants had to agree to discontinue any other therapy or treatment	Having another psychiatric disorder with a higher clinician severity than for SocAD; lack of motivation.	Primary target SocAD: 100% Comorbid conditions Specific phobias: 40% GAD: 21% SepAD: 12% OCD: 4% Panic disorder (±) agoraphobia: 3% MDD: 12% Neurodevelopmental disorders: 7% ODD: 2%

	Patient Characteristics: Age, Mean (SD)			
Author, Year, Registry Number	Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Perrin et al, 2019 ¹²²	Mean age (SD):	Ages 10 to 18 years,	No other exclusion criteria were	Primary Condition GAD %
ISRCTN50951795	IG1: 13.2 (2.4)	referred for treatment of	applied.	IG1: 100%
	CG: 13.6 (2.8)	anxiety with a current and		CG: 100%
	, ,	primary diagnosis of DSM-		Comorbid conditions %
	N (%) Female:	IV GAD with no other		SepAD
	IG1: 11 (55)	psychiatric problems in		IG1: 40%
	CG: 14 (70)	need of more urgent		CG: 10%
		treatment, including self-		SocAD
	Race/Ethnicity:	injurious thoughts or		IG1: 10%
	Ethnic minority	behaviors or substances		CG: 35%
	IG1: 5 (25)	use/abuse, no concurrent		Specific phobia
	CG: 6 (30)	psychological or		IG1: 5%
		pharmacological treatment		CG: 0%
		for any disorders, and the absence of moderate to		MDD IG1: 15%
		severe learning difficulties		CG: 15%
		as evidenced in medical or		00. 1070
		school records or reported		
		by the referrer or parent.		
Pine et al, 2001 ¹²⁴	Mean age (SD):	Ages 6 to 17 years, meet	Current	Diagnoses at baseline
Walkup et al, 2001 ²¹³	IG1: 10.4 (2.8)	criteria for socAD, sepAD,	psychopharmacotherapy;	SepAD: 59%
Ginsburg et al,	CG: 10.3 (3.1)	or GAD using DSM-IV,	current diagnosis of major	GAD: 57%
2006 ²¹⁴	N (%) ages 6 to 12 years	clinically important anxiety	depression, Tourette's	SocAD: 66%
Reinblatt et al,	IG1: 48 (76)	symptoms as measured by	syndrome, OCD, PTSD, panic	Past or current comorbid conditions
2009 ²¹⁵	CG: 47 (72)	the PARS, Children's	disorder, or ADHD that required	ADHD: 16%
	N (0() Fara alay 00 (40)	Global Assessment Scale	drug therapy; history or current	ODD: 5%
	N (%) Female: 63 (49)	score <60, and willingness	diagnosis of mania, psychosis, or PDD; current suicidal	MDD: 5% PTSD: 2%
	Race/Ethnicity:	to attend clinic weekly.	ideation; mental retardation;	F13D. 270
	White: 81 (63)		and previous treatment with an	
	Black: 9 (7)		SSRI.	
	Hispanic: 24 (19)		33141.	
	Other: 14 (11)			

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Rudy et al, 2017 ¹²⁹ NCT02051192	Mean age (SD): 5.36 (1.14) N (%) Female: 9 (41) Race/Ethnicity: White: 14 (64) Hispanic: 3 (14) Black: 1 (5) Asian: 1 (5) Other: 3 (14)	Ages 4 to 7 years meeting DSM-IV-TR criteria for a diagnosis of an anxiety disorder or a minimum score of 12 on the PARS and a score ≥70 on the PPVT-IV. Participants taking prescribed psychotropic medication must have been stable (no change in dose or type) for 10 weeks prior to entering the study.	No additional criteria.	Target conditions: SocAD: 23% OCD: 23% SepAD: 14% Selective mutism: 9% Specific phobia: 9% GAD: 5% Anxiety NOS: 5%: Other comorbid conditions ADHD: 45% Disruptive behavioral disorder: 32%
Rynn et al, 2001 ¹³⁰	Mean age (SD): 11.7 (3.9) N (%) Female: 5 (22.7) Race/Ethnicity: White: 18 (81)	Ages 5 to 17 years meeting DSM-IV criteria for GAD according to the ADIS for Children–Revised, and a Hamilton Anxiety Rating Scale score ≥16	Acute or unstable medical conditions such as diabetes, seizure disorder, severe asthma, or hyperthyroidism; additional axis I or axis II psychiatric disorder, such as MDD, OCD, mental retardation, PDD, eating disorder, schizophrenia, or other psychotic disorders; comorbid ADHD and oppositional defiant disorder; at risk for suicide and/or had abnormal results on the physical examination or laboratory tests.	GAD: 100% Subsyndromal sepAD: 27%
Salzer et al, 2018 ⁴² , ISRCTN 22752528	Mean age (SD): 17.4 (2.0) N (%) Female: 71 (66) Race/Ethnicity: NR	Ages 14 to 20 years with a primary diagnosis of SocAD based on German edition of Kiddie-SADS-Present and Lifetime version.	Psychotic and acute substance- related disorders, organic mental disorders, severe medical conditions, ADHD, PTSD, suicidal ideation; IQ <80; or concurrent psychotherapeutic or psychopharmacological treatments.	Primary/target condition SocAD: 100% Other comorbid conditions Specific phobia: 27% MDD: 24% Dysthymia: 12% GAD: 8%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Sanchez-Garcia et al, 2009 ¹³¹ NR	Mean age (SD): 11.91 (1.3) N (%) Female: 60 (73) Race/Ethnicity: NR	Age 10 to 14 years meeting ADIS-IV criteria for generalized social phobia	Failure to attend three consecutive sessions.	NR
Shortt et al, 2001 ¹³⁴	Mean age (SD): 7.9 (1.2) N (%) Female: 42 (59) Race/Ethnicity: Australian: NR (92%) European: NR (7%) Asian: NR (1%)	Ages 6 to 10 years, with one or more of the following principal anxiety disorder diagnoses: GAD, SocAD, or SepAD	Intellectual or severe physical impairment, or currently receiving psychosocial or psychopharmacological interventions.	Primary target condition GAD: 59% SocAD: 14% SepAD: 27% Other comorbid conditions Comorbid GAD: 20% Comorbid specific phobia: 38% Comorbid Sep AD: 16% Comorbid SocAD: 13% Dysthymia: 3% Major depression: 1%
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	Mean age (SD): 15 (1.3) N (%) Female: 55 (79) Race/Ethnicity: NR	Ages 13 to 17 years with diagnosis for primary anxiety disorder according to DSM-IV and who had direct access to a home computer with internet access	Severe comorbid depression, substance abuse, current severe self-harm or suicidal ideation, pervasive developmental disorder, learning disorder or intellectual disability, or psychotic symptoms.	Primary diagnosis SocAD: 40% GAD: 16% Specific phobia: 9% SepAD: 13% PD: 4% PD with agoraphobia: 3% Agoraphobia without PD OCD: 11% (considered as a primary anxiety diagnosis at time of study) Number of comorbid anxiety diagnoses: mean 2.11 (SD 0.93) Other comorbid diagnoses Other anxiety disorder: 73% Mood disorder: 9%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Strawn et al, 2015 ¹⁴² NCT01226511	Mean age (SD): IG1: 12.6 (3.0) CG: 12.2 (2.9) N (%) Female: IG: 70 (51.9) CG: 75 (54.7) Race/Ethnicity: IG: White: 112 (83.0) Black: 9 (6.7) Multiracial: 6 (4.4) American Indian or Alaska Native: 7 (5.2) Asian: 1 (0.7) Hispanic or Latino: 37 (29.6) CG: White: 111 (81.0) Black: 10 (7.3) Multiracial: 9 (6.6) American Indian or Alaska Native: 6 (4.4) Asian: 1 (0.7) Hispanic or Latino: 40 (31.3)	Ages 7 to 17 years meeting DSM-IV-TR criteria for GAD, assessed using the MINI-Kid, and had a PARS severity for GAD score 15 at two screening visits; CGI-Severity score ≥4 at the two screening visits; and significant social, academic, and/or familial dysfunction as determined by CGAS score of ≤60 at two screening visits	Current MDD or history of bipolar disorder, psychotic disorder, eating disorder, OCD, posttraumatic stress disorder, or panic disorder, had a first-degree relative with bipolar I disorder, represented a serious suicide risk, or had a history of substance abuse/dependence within the past year or an unexplained positive urine drug screen. Current use of antidepressants, antipsychotics, anticonvulsants, anorexics, benzodiazepines, psychostimulants (excluding caffeine), and herbal preparations with central nervous system activity.	SepAD: 18.75% SocAD: 17.65%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Strawn et al, 2020 ¹⁴³ NCT02818751	Mean age (SD): IG1: 14.8 (1.7) CG: 14.9 (1.6) N (%) Female: IG1: 20 (77) CG: 19 (76) Race/Ethnicity: IG1: Asian: 0 (0) Black or African American: 1 (4) White: 23 (88) Other: 2 (8) Hispanic or Latino: 3 (12) CG: Asian: 2 (8) Black or African American: 1 (4) White: 20 (80) Other: 2 (8) Hispanic or Latino: 0 (0)	Ages 12 to 17 years, DSM-IV-TR criteria for GAD assessed using ADIS, PARS score ≥15 and a CGI-S score ≥4	Current MDD or any history of DSM-IV-TR bipolar disorder, psychotic disorder, OCD, or PTSD. Use of antidepressants, antipsychotics, anticonvulsants, stimulants, or benzodiazepines was prohibited.	Primary/target condition % GAD: 100% Comorbid conditions % SepAD: 17.6% Panic disorder: 56.9% Agoraphobia: 27.5% ADHD: 17.6% Specific phobia: 3.5%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	Mean age (SD): NR N (%) Female: IG1: 30 (49) IG2: 30 (47) CG: 34 (49) Race/Ethnicity: IG1 White: 53 (87) IG2 White: 55 (86) CG White: 58 (84)	Ages 7 to 12 years meeting DSM-IV criteria for GAD, SocAD, SepAD, panic disorder, agoraphobia, or specific phobia and primary caregiver available to attend treatment. If taking psychotropic medication, stable dosage for at least 1 month and agreement to maintain dose throughout study.	Significant physical or intellectual impairment (including ASD) in the participating child and significant intellectual impairment or current DSM-IV anxiety disorder or other severe mental health difficulties (MDD, psychosis, substance/alcohol dependence) in the primary caregiver.	Primary condition IG1 SepAD: 23% SocAD: 18% GAD: 26% Other: 33% IG2 SepAD: 25% SocAD: 20% GAD: 25% Other: 30% CG SepAD: 22% SocAD: 25% GAD: 25% GAD: 25% GAD: 25% GAD: 25% GAD: 12% Other: 32% Other comorbid conditions IG1 PDD: 2% MDD: 8% ADHD: 12% ODD: 15% IG2 PDD: 5% MDD: 3% ADHD: 8% ODD: 14% CG PDD: 6% MDD: 10% ADHD: 12% ODD: 16%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Villabo et al, 2018 ¹⁵⁰ NR	Mean age (SD): 10.5 (1.5) N (%) Female: 75 (45.5) Race/Ethnicity: Caucasian: 163 (98.8) Asian: 1 (0.6) Hispanic: 1 (0.6)	Ages 7 to 13 years with a primary DSM-IV diagnosis of SepAD, GAD, or SocAD, significant functional impairment, an IQ of 70 or higher, and at least one parent proficient in Norwegian.	A mental health disorder with a higher treatment priority, PDD, psychosis, or current use of anxiolytic medication.	Other comorbid conditions % MDD: 3% Specific phobia: 27% ADHD: 19% ODD: 7%
Waite et al, 2019 ¹⁵² ISRCTN79652741	Mean age (SD): 14.7 (1.42) N (%) Female: 39 (65) Race/Ethnicity: White: 55 (92)	Adolescents ages 13 to 18 years and their parents with a DSM-IV anxiety disorder diagnosis identified as the primary problem	Diagnosis of OCD, if on medication, on stable dose for 2 months and agree to remain on that dose for the trial, parent with no significant intellectual impairment, psychotic symptoms, substance dependence, conduct d/o, autism, learning problems, self-harm behaviors within previous month, or computer and internet access at home.	Primary/target condition % SocAD: 19 (32) GAD: 15 (25) SepAD: 5 (8) Panic with agoraphobia: 7 (12) Panic without agoraphobia: 1 (2) Agoraphobia: 2 (3) Specific phobia: 11 (18) Other comorbid conditions % Dysthymia: 10 (17) MDD: 3 (5) ADHD: 1 (2) ODD: 2 (3) School refusal: 7 (12)

Appendix I Table 18. Anxiety Treatment Studies: Population Characteristics (KQ 4)

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/Behavioral Conditions
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	Mean age (SD): 10.7 (2.8) N (%) Female: 242 (50) Race/Ethnicity: White: 385 (79) Black: 44 (9) Asian: 12 (3) American Indian: 6 (1) Pacific Islander: 2 (0) Other: 39 (8) Hispanic: 59 (12)	Ages 7 to 17 years with a primary diagnosis of SepAD, GAD, or SocAD using DSM-IV-TR criteria, substantial impairment, and an IQ ≥80. Children with comorbid psychiatric diagnosis of lesser severity than the target disorders were also included.	Unstable medical conditions; refusal to attend school because of anxiety; failure to have a response to two adequate trials of SSRIs or one adequate trial of CBT; pregnancy or unprotected sexual activity in females; psychoactive medications other than stable stimulant medication; psychiatric diagnosis such as MDD, substance use disorder, unmedicated ADHD, lifetime history of bipolar disease, psychotic disorders, or PDD; those who presented as acute risk to themselves or others.	Primary/target conditions SepAD: 3% SocAD: 11% GAD: 7% SepAD and SocAD: 7% SepAD and GAD: 8% SocAD and GAD: 28% SepAD, SocAD, and GAD: 36% Other comorbid conditions Other internalizing disorder: 44% ADHD: 12% ODD or conduct disorder: 9% Tic disorder: 3%

Abbreviations: ADHD=attention deficit hyperactivity disorder; ADHD= attention deficit—hyperactivity disorder; ADIS=Anxiety Disorders Interview Schedule; ADIS-C=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children; ADIS-IV=Anxiety and Related Disorders Interview Schedule-IV?; ASD=autism spectrum disorder; CBT=cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CGI=Clinical Global Impressions; CGI-S= Clinical Global Impressions=Severity; CSR=Clinician Severity Rating; DSM=DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 5th Edition; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision; GAD=generalized anxiety disorder; IG=intervention group; IQ=intelligent quotient; KQ=key question; MDD=major depressive disorder; MINI=Mini International Neuropsychiatric Interview; NA=not available; NOS=not otherwise specified; NR=not reported; OCD=obsessive compulsive disorder; ODD=oppositional defiant disorder; PARS=Pediatric Anxiety Rating Scale; PD=panic disorder; PDD=persistent depressive disorder; PPVT-IV= Peabody Picture Vocabulary Test; PTSD=post-traumatic stress disorder; SAD=suicide, anxiety, depression; SD=standard deviation; SepAD=separation anxiety disorder; SocAD=social anxiety disorder; SP=social phobia; SSRI=selective serotonin reuptake inhibitor

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Anxiety Symptoms
Arendt et al, 2016 ⁶⁵	IG1: Group child + parent in-person CBT (N=56) CG: Wait-list (N=53)	ADIS CSR primary diagnosis, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 2.16 (2.59) CG: 5.45 (1.90) Time-by-condition effect, P<0.001, partial eta squared=0.35 ADIS CSR all diagnosis, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 5.21 (5.19) CG: 10.75 (5.63) Time-by-condition effect, P<0.001, partial eta squared=0.22
		SCAS-youth, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 21.57 (14.42) CG: 32.55 (15.64) Time-by-condition effect, P<0.001, partial eta squared=0.18
		SCAS-P mother, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 22.25 (12.59) CG: 37.04 (16.95) Time-by-condition effect, P<0.001, partial eta squared=0.24
		SCAS-P father, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 23.56 (13.87) CG: 32.63 (16.17) Time-by-condition effect, P<0.001, partial eta squared=0.19
Asbrand et al, 2020 ⁶⁷ TU 78/5-2, HE 3342/4-2	IG1: Group child- focused in-person CBT (N=31) CG: WLC (N=36)	SPAI-C, posttreatment (12 weeks), ITT (IG1=31; CG=36), Time x Group interaction No group effect, F(2,116.6)=5.87, p=0.899, but a significant interaction effect of Time x Group F(2,116.6)=5.87, p=0.004 favoring CBT
		SASC-R Child, posttreatment (12 weeks), ITT (IG1=31; CG=36), Time x Group interaction No main effect of Group, F(1,66)=0.39, p=0.534 or Time x Group interaction F(2,115.6)=1.16, p=0.316 SASC-R Parent, posttreatment (12 weeks), ITT (IG1=31; CG=36), Time x Group interaction No main effect of group, F(1,65.2)=0.27, p=0.608 or Time x Group interaction F(2,114.4)=1.01, p=0.366
Barrett et al, 1996 ⁷⁰	IG1: CBT (N=28) IG2: CBT + family intervention (N=25) CG: Wait-list (N=26)	RCMAS, posttreatment (12 weeks), completer (IG1=28; CG=23), mean (SD) IG1: 9.0 (6.8) CG: 11.6 (6.0) Time x treatment interaction=NS
		RCMAS, posttreatment (12 weeks), completer (IG2=25; CG=23), mean (SD) IG2: 6.6 (4.6) CG: 11.6 (6.0) Time x treatment interaction=NS

Author Voor Bogistm	Treatment Interventions and	
Author, Year, Registry Number	Comparators	Anxiety Symptoms
Barrett et al, 1996 ⁷⁰		FSSCR, posttreatment (12 weeks), completer (IG1=28; CG=23), mean (SD)
(continued)		IG1: 119.9 (26.0)
		CG: 134.3 (32.6)
		Time x Treatment interaction=NS
		FSSCR, posttreatment (12 weeks), completer (IG2=25; CG=23), mean (SD)
		IG2: 114.2 (20.2)
		CG: 134.3 (32.6)
		Time x Treatment interaction=NS
Birmaher et al, 2003 ⁷³	IG1: Fluoxetine (N=37)	SCARED-C, posttreatment (12 weeks), ITT (IG1=37, CG=37), mean (SD)
	CG: Placebo (N=37)	IG1: 11.7 (12.4) CG: 14.6 (14.5)
		Time x Treatment baseline to 12 weeks p=0.03
		Timo X Trodumont basonito to 12 woode p-olos
		SCARED-P, posttreatment (12 weeks), ITT (IG1=37, CG=37), mean (SD)
		IG1: 16.3 (12.7)
		CG: 22 (12.3)
		Time x Treatment baseline to 12 weeks p=0.04
		PARS, posttreatment (12 weeks), ITT (IG1=37, CG=37), mean (SD)
		IG1: 7.1 (5.9)
		CG: 9.3 (4.8)
		Time x Treatment baseline to 12 weeks p=0.04
		CGI-S ≤4, posttreatment (12 weeks) (IG1=37, CG=37), % (SD)
		IG1: 89.3 (0.06)
		CG: 83.9 (0.07)
		Time x Treatment baseline to 12 weeks p=0.007
Black et al, 1994 ⁷⁴	IG1: Fluoxetine (N=6)	CGI anxiety parent-rated marked or much improved, posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%)
	CG: Placebo (N=9)	IG1: 2 (33.3) CG: 1 (11.1)
		p=NS
		CGI generalized anxiety clinician-rated marked or much improved; posttreatment (12 weeks), ITT (IG1=6; CG=9), N
		(%)
		IG1: 4 (66.7)
		CG: 3 (33.3) p=NS
		CGI social anxiety clinician-rated marked or much improved; posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%)
		IG1: 4 (66.7)
		CG: 5 (55.6)

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
	•	p=NS
Black et al, 1994 ⁷⁴ (continued)		CGI anxiety teacher-rated marked or much improved; posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%) IG1: 5 (83.3) CG: 6 (66.7) p=NS
Cobham et al, 2017 ⁷⁷ ACTRN12615000514505	IG1: Group parent-only in-person CBT (N=33) CG: Wait list control (N=30)	ADIS-CSR, posttreatment (6 weeks), mITT(IG1=33; CG=29), mean (SD) IG1: 3.7 (2.6) CG: 5.4 (1.1) Between-group difference in change from baseline; P<0.001 SCAS-M, posttreatment (6 weeks), mITT(IG1=33; CG=29), mean (SD) IG1: 20.1 (4.9) CG: 32.3 (11.9) Between-group difference in change from baseline; P<0.001 SCAS-F, posttreatment (6 weeks), mITT (IG1=33; CG=29), mean (SD) IG1: 21.4 (14.4) CG: 30.6 (15.2) Between-group difference in change from baseline; p=0.53 SCAS-C, posttreatment (6 weeks), mITT (IG1=33; CG=29), mean (SD) IG1: 34.4 (13.9) CG: 42.1 (11.5) Between-group difference in change from baseline; P<0.01
Cornacchio et al, 2019 ⁷⁹ NA	IG1: Group child+parent in-person CBT (N=14) CG: Wait list control (N=15)	ADIS CSR selective mutism, posttreatment (4 weeks), ITT (IG1=14; CG=15), Mean (SD) IG1: 4.2 (0.9) CG: 4.6 (0.7) Time x Condition interaction P>0.05 Effect size Cohen's d=-0.50 ADIS CSR social anxiety, posttreatment (4 weeks), ITT (IG1=14; CG=15), Mean (SD) IG1: 4.0 (0.8) CG: 3.6 (1.5) Time x Condition interaction P<0.05 Effect size Cohen's d=-0.50 SMQ-P home subscale, posttreatment (4 weeks), ITT (IG1=14; CG=15), Mean (SD) IG1: 2.2 (0.4) CG: 1.7 (0.7) P>0.05 Cohen's d=0.36

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Anxiety Symptoms
Cornacchio et al, 2019 ⁷⁹ NA (continued)		SMQ-P social subscale, posttreatment (4 weeks), ITT (IG1=14; CG=15), Mean (SD) IG1: 1.2 (0.6) CG: 0.7 (0.7) P<0.05 Cohen's d=0.58
Donovan et al, 2014 ⁸³ ACTRN12612000139875	IG1: Individual parent- focused internet CBT (N=23) CG: Wait-list (N=29)	CSR, posttreatment (8 weeks), mITT (IG1=23; CG=27), Mean (SD) IG1: 3.4 (2.4) CG: 4.7 (2.0) Time x treatment p=0.002, partial eta squared 0.176 For ITT population: Time x Treatment p=0.001, partial eta squared=0.188 PAS, posttreatment (8 weeks), mITT (IG1=19; CG=29), Mean (SD) IG1: 30.0 (14.7) CG: 40.2 (17.0) Time x Treatment p=0.011, partial eta squared=0.131 For ITT population: Time x Treatment p=0.66, partial eta squared=0.066
Ginsburg et al, 2020 ⁹²	IG1: Individual child- focused in-person CBT (N=148) CG: TAU (N=68)	CGI-S, posttreatment (12 weeks), ITT (IG=148; CG=68), mean IG: 3.97 CG: 4.15 p=0.38 CGI-S, 12 months, ITT (IG=148; CG=68), mean IG: 3.61 CG: 3.41 p=0.34 SCARED-P, posttreatment (12 weeks), ITT (IG=148; CG=68), mean IG: 20.25 CG: 21.72 Cohen's d=0.29; p=0.05 SCARED-P, 12 months, ITT (IG=148; CG=68), mean IG: 17.74 CG: 15.12 p=0.44 SCARED-C, posttreatment (12 weeks), ITT (IG=148; CG=68), mean IG: 22.82 CG: 23.65 p=0.87

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Ginsburg et al, 2020 ⁹²	•	SCARED-C, 12 months, ITT (IG=148; CG=68), mean
(continued)		IG: 19.63 CG: 20.54
		p=0.65
Hirshfeld-Becker et al,	IG1: Individual child +	CGI-I SocAD score, posttreatment (6 months), completers (IG1=19, CG=20), mean (SD)
201098	parent in-person CBT	IG1: 2.42 (0.96)
	(N=34) CG: Wait-list control (N=30)	CG: 3.40 (1.05) P<0.01; Hedge's g=0.95 (95% CI, 0.29 to 1.62)
	(** 33)	CGI-I SepAD score, posttreatment (6 months), completers (IG1=12; CG=13), mean (SD) IG1: 1.67 (0.98)
		CG: 2.46 (0.88) p=0.045; Hedge's g=0.82 (95% CI, 0.01 to 1.64)
		CGI-I GAD score, posttreatment (6 months), completers (IG1=12; CG=12), mean (SD) IG1: 2.17 (0.83) CG: 2.58 (1.38) p=0.38; Hedge's g=NR
		CGI-I specific phobia score, posttreatment (6 months), completers (IG1=15; CG=15), mean (SD) IG1: 1.87 (1.30) CG: 2.87 (1.19) p=0.037; Hedge's g=0.78 (95% CI, 0.04 to 1.52)
		CGI-I agoraphobia score, posttreatment (6 months), completers (IG1=9; CG=11), mean (SD) IG1: 2.22 (0.83) CG: 2.55 (1.45) p=0.58
Holmes et al, 201499	IG1: Group child-	ADIS-C/P CSR, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD)
ACTRN12612000061831	focused in-person CBT (N=20)	IG1: 3.59 (1.3) CG: 6.21 (0.79)
	CG: Wait-list control (N=22)	P<0.001, partial eta squared=0.43
	,	SCAS-P GAD symptoms, posttreatment (10 weeks), ITT (IG1=20, CG=22), mean (SD) IG1: NR CG: NR
		Time x Group interaction: p=0.048, partial eta squared=0.09

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Anxiety Symptoms
Holmes et al, 2014 ⁹⁹ ACTRN12612000061831 (continued)		SCAS-P GAD symptoms, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 6.17 (2.71) CG: 6.84 (2.29) Time x Group interaction: p=0.053
		SCAS-P total symptoms, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 29.94 (12.70) CG: 31.47 (8.79) Time x Group interaction: p=NS
		SCAS-C GAD symptoms, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 7.41 (4.65) CG: 8.42 (4.56) Time x Group interaction: p=NS
		SCAS-C total symptoms, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 34.88 (20.25) CG: 40.84 (19.93) Time x Group interaction: p=NS
Ishikawa et al, 2019 ¹⁰³	IG1: Individual child + parent in-person CBT (N=26) CG: Wait-list (N=25)	SCAS-C, posttreatment (2 or 4 months), completers (IG=25; CG=24), mean (SE) IG: 28.28 (3.55) CG: 35.95 (3.97) Time x Treatment interaction: p=NS
		ADIS-DSM-IV CSR, posttreatment (2 or 4 months), ITT (IG=25; CG=24), mean (SE) [on primary diagnosis] IG: 3.08 (0.50) CG: 6.0 (0.51) Time x Treatment interaction: P<0.001 favoring CBT
		SCAS-P, posttreatment (2 or 4 months), completers (IG=25; CG=24), mean (SE) IG: 25.42 (2.57) CG: 27.57 (2.62) Time x Treatment interaction: P<0.01 favoring CBT
Lau et al, 2010 ¹¹⁰ NR	IG1: Group child + parent in-person CBT (N=26) CG: Wait-list control (N=25)	SCAS, posttreatment (13 weeks), mITT (IG1=24; CG=21), mean (SD) IG1: 24.6 (10.5) (9.7 decrease from baseline) CG: 38.8 (13.7) (1.8 increase from baseline) Effect size partial eta squared=0.27 Time x Condition interaction: P<0.001
		PSCAS, posttreatment (13 weeks), mITT (IG1=24; CG=21), mean (SD) IG1: 28.8 (10.3) (4.2 decrease from baseline)

Treatment nterventions and Comparators	Anxiety Symptoms
	CG: 36.5 (11.0) (1.3 increase from baseline) Effect size partial eta squared=0.11 Time x Condition interaction: P<0.05
1: Parent-guided BT supported by ephone (N=28) 2: Parent-guided BT supported by nail (N=21) 3: Parent-guided BT with as needed poort (N=29) 6: Wait-list (N=22)	Time x Condition interaction: P<0.05 ADIS CSR (sum of all anxiety disorders), posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22) IG1 vs. CG: Effect size cohen's d: 2.19, P<0.01 IG2 vs. CG: Effect size cohen's d: 0.157, P<0.01 IG3 vs. CG: Effect size cohen's d: 0.80, P<0.01 Time x Treatment interaction across all groups: eta squared=0.49; P<0.01 SCAS-M, pretreatment, ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 39.50 (14.94) IG2: 36.00 (14.57) IG3: 34.97 (15.50) CG: 39.23 (13.89) SCAS-M, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 20.36 (16.04) IG2: 21.29 (14.28) IG3: 22.97 (15.20) CG: 37.77 (15.26) SCAS-F, pretreatment, ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 32.46 (14.48) IG2: 26.47 (9.91) IG3: 29.80 (16.90) CG: 28.33 (17.68) SCAS-F, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 22.50 (13.48) IG2: 18.76 (10.37) IG3: 19.60 (13.45) CG: 29.50 (18.39) SCAS-C, pretreatment, ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 43.54 (16.65) IG3: 35.90 (12.13) IG3: 35.90 (12.13) IG3: 35.90 (12.13)
1:37 2:37 3:37 9:18	Comparators : Parent-guided supported by supported by Parent-guided supported by supported by sil (N=21) Parent-guided with as needed port (N=29)

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Anxiety Symptoms
Lyneham et al, 2006 ¹¹² NR (continued)		SCAS-C, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 23.79 (14.84) IG2: 24.86 (12.94) IG3: 25.79 (19.51) CG: 36.41 (21.87)
		RCMAS-C, pretreatment, ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 17.25 (5.72) IG2: 14.14 (6.35) IG3: 14.17 (7.48) CG: 15.59 (7.57)
		RCMAS-C, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 10.89 (6.55) IG2: 8.67 (6.21) IG3: 10.28 (7.66) CG: 15.73 (7.30)
Ost et al, 2015 ¹²⁰	IG1: Individual + group child (N=16) IG2: Child + parent in- person CBT (N=16) CG: Wait-list (N=23)	Change in CSR from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD) IG1: 3.25 (0.39) IG2: 3.69 (1.66) CG: 5.95 (1.15) Time x Treatment: F=26.6, P<0.001. IG1 vs. CG: p=sig, NR, favoring IG1 IG2 vs. CG: p=sig, NR, favoring IG2
		Change in SPAI-C from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD) IG1: 12.5 (8.9) IG2: 19.1 (12.0) CG: 22.8 (9.4) Time x Treatment: F=5.0, P<0.05 IG1 vs. CG: p=sig, NR, favoring IG1 IG2 vs. CG: p=sig, NR, favoring IG2
		Change in MASC from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD) IG1: 35.8 (16.0) IG2: 43.2 (18.1) CG: 54.7 (15.3) Time x Treatment: F=4.6, P<0.05 IG1 vs. CG: p=sig, NR, favoring IG1 IG2 vs. CG: p=NS

Author, Year, Registry	Treatment Interventions and	Associate Occupations
Number Ost et al, 2015 ¹²⁰	Comparators	Anxiety Symptoms Change in SPAI-P from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD)
(continued)		IG1: 19.8 (10.7)
(continued)		IG2: 24.6 (12.5)
		CG: 29.8 (8.7)
		Time x Treatment: F=4.2, P<0.05
		IG1 vs. CG: p=sig, NR, favoring IG1
		IG2 vs. CG: p=NS
		Change in FSSCR from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD)
		IG1: 109.1 (23.7)
		IG2: 117.3 (30.2) CG: 119.3 (32.6)
		Time x Treatment: F=0.8, P>0.05
		IG1 vs. CG: p=NS
		IG2 vs. CG: p=NS
Perrin et al, 2019 ¹²²	IG1: Individual child +	ADIS GAD severity, posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD)
ISRCTN50951795	parent in-person +	IG1: 1.9 (2.3)
	internet CBT (N=20)	CG: 5.7 (1.1)
	CG: Wait-list control (N=20)	Effect size partial eta squared=0.54 p<0.001
	(N=20)	p<0.001
		SCARED-R-C (anxiety), posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD)
		IG1: 15.2 (12.5)
		CG: 46.3 (15.9)
		Effect size partial eta squared=0.53
		p<0.001
		SCARED-R-P (anxiety), posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD)
		IG1: 18.9 (12.4)
		CG: 38.2 (14.9)
		Effect size partial eta squared=0.37 p<0.001
		ρ<0.001
		SCARED-R-C (GAD), posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD)
		IG1: 4.6 (5.2)
		CG: 12.9 (4.2) Effect size partial eta squared=0.47
		p<0.001
		SCARED-R-P (GAD), posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD)
		SCARED-R-P (GAD), posttreatment (10 weeks), 111 (IG1=20, CG=20), mean (SD)
		CG: 11.2 (4.7)

	Treatment	
Author, Year, Registry	Interventions and	
Number	Comparators	Anxiety Symptoms
		Effect size partial eta squared=0.24 p<0.001
		PSWQ-C, posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD) IG1: 10.6 (12.2)
		CG: 31.1 (7.2)
		Effect size partial eta squared=0.54 P<0.001
Pine et al, 2001 ¹²⁴	IG1: Fluvoxamine	PARS change in score, baseline to posttreatment (8 weeks), mITT (IG1=61; CG=63), mean (SD)
Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴	(N=63) IG2: Sertraline	IG1: 9.0 (7.0) CG: 15.9 (5.3)
Reinblatt et al, 2009 ²¹⁵	(N=133)	Time x Treatment interaction: P<0.001
	IG3: CBT + sertraline (N=140)	
	CG: Placebo (N=65)	
Rudy et al, 2017 ¹²⁹ NCT02051192	IG1: Individual parent-	ADIS CSR, posttreatment (5 weeks), ITT (IG1=12; CG=10), mean (SD)
NC102051192	led in-person CBT (N=12)	IG1: 2.72 (1.56) CG: 4.56 (1.81)
	CG: TAU (N=10)	Time x Treatment interaction: effect size d=2.39, p=0.009
		CGI-S, posttreatment (5 weeks), ITT (IG1=12; CG=10), mean (SD) IG1: 2.00 (0.89)
		CG: 3.33 (0.71)
		Time x Treatment interaction: effect size d=2.75, P<0.001
		PARS, posttreatment (5 weeks), ITT (IG1=12; CG=10), mean (SD) IG1: 9.72 (4.76)
		CG: 15.78 (3.35)
Rynn et al, 2001 ¹³⁰	IG1: Sertraline (N=11)	Time x Treatment interaction: effect size d=3.18, p=0.046 HAM-A, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD)
Tryfiir Ct ai, 2001	CG: Placebo (N=11)	IG: 7.8 (5.7)
		CG: 21.0 (7.8)
		P<0.001 Time x Treatment interaction: baseline to posttreatment P<0.001
		·
		CGI-S, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 2.4 (0.8)
		CG: 3.9 (0.3)
		P<0.001
		Time x Treatment interaction: baseline to posttreatment P<0.001

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Rynn et al, 2001 ¹³⁰ (continued)		CGI-I, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 2.1 (1.1) CG: 3.5 (0.7) p=0.001 Time x Treatment interaction: baseline to posttreatment P<0.001
		ADIS CSR-C posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 2.7 (2.0) CG: 4.6 (2.0) p=0.11
		ADIS CSR-P, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 2.6 (1.7) CG: 4.9 (2.0) P<0.007
		RCMAS, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 8.9 (7.0) CG: 14.6 (8.2) P<0.02
		MASC total score, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 35.7 (17.2) CG: 56.4 (16.3) P<0.03
Salzer et al, 2018 ^{42,} ISRCTN 22752528	IG1: Individual child- focused in-person CBT (N=34) CG: Wait-list control (N=39)	LSAS-CA, change in score from baseline to posttreatment, ITT (IG1=34; CG=39), effect size Cohen's d=0.61 (95% CI, 0.14 to 1.08); p=0.0112 SPAI, change in score from baseline to posttreatment, ITT (IG1=34; CG=39), effect size Cohen's d=0.75 (95% CI, 0.27 to 1.22); p=0.0021
Sanchez-Garcia et al, 2009 ¹³¹ NR	IG1: Individual + group child-focused inperson CBT (N=28) IG2: Group CBT without cognitive restructuring (N=29) CG: Wait-list control (N=25)	SPAI-C, posttreatment (12 weeks), mITT (IG1=28, IG2=29, CG=25), mean (SD) IG1: 15.45 (7.77) IG2: 12.75 (8.03) CG: 30.80 (5.75) IG1 vs. CG P<0.001, effect size 2.23 (unclear what type of ES this is) IG2 vs. CG P<0.001, effect size 2.51 (unclear what type of ES this is)

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Sanchez-Garcia et al, 2009 ¹³¹ NR (continued)		SPAI-C, 6 months, mITT (IG1=28, IG2=29, CG=25), mean (SD) IG1: 11.91 (6.03) IG2: 13.21 (8.55) CG: 27.64 (4.01) IG1 vs. CG P<0.001, effect size 3.04 (unclear what type of ES this is) IG2 vs. CG P<0.001, effect size 2.08 (unclear what type of ES this is) SASC-R, posttreatment (12 weeks), mITT (IG1=28, IG2=29, CG=25), mean (SD) IG1: 15.89 (6.81) IG2: 11.45 (6.48) CG: 35.36 (5.33)
Chart at al 0004134	ICA Crown shild	IG1 vs. CG P<0.001, effect size 3.16 (unclear what type of ES this is) IG2 vs. CG P<0.001, effect size 3.94 (unclear what type of ES this is) SASC-R, 6 months, mITT (IG1=28, IG2=29, CG=25), mean (SD) IG1: 12.14 (6.86) IG2: 12.24 (7.34) CG: 38.80 (6.71) IG1 vs. CG P<0.001, effect size 2.44 (unclear what type of ES this is) IG2 vs. CG P<0.001, effect size 2.90 (unclear what type of ES this is)
Shortt et al, 2001 ¹³⁴	IG1: Group child + parent in-person CBT (N=54) CG: Wait-list (N=17)	RCMAS posttreatment (10 weeks), completers (IG1=53 CG=12), mean (SD) IG1: 8.6 (0.97) CG: 9.8 (2.0) Time x Treatment, eta squared=0.10, P<0.05 DISCAP CSR, posttreatment (10 weeks), completers (IG1-48, CG-16), mean (SD) IG1: 1.06 (0.24) CG: 4.13 (0.41) Time x Treatment, eta squared=0.46, P<0.001
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	IG1: Individual child- focused internet CBT (N=35) CG: Wait-list control group (N=35)	ADIS-DSM-IV CSR (primary diagnosis), change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.65; p=0.022 ADIS-DSM-IV CSR (all anxiety diagnoses), change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.83; p=0.002 SCAS-C, change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.68; P<0.001

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
		SCAS-M change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=1.12; P<0.001 SCAS-F change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect
		size Cohen's d=0.46; p=0.011
Strawn et al, 2015 ¹⁴² NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	PARS severity for GAD, mean change from baseline to post acute treatment (10 weeks), ITT (IG=135; CG=133), mean (SE) IG: -9.7 (0.5) CG: -7.1 (0.5) d=0.5 P≤0.001, favoring duloxetine
		PARS severity total score, mean change from baseline to post acute treatment (10 weeks), ITT (IG=135; CG=133), mean (SE) IG: -9.2 (0.5) CG: -6.4 (0.5) P≤0.001, favoring duloxetine
		CGI-S mean change from baseline to post acute treatment (10 weeks), ITT (IG=135; CG=133), mean (SE) IG: -1.9 (0.1) CG: -1.4 (0.1) P≤0.001, favoring duloxetine
Strawn et al, 2020 ¹⁴³ NCT02818751	IG1: Escitalopram (N=26) CG: Placebo (N=25)	PARS, score from baseline to posttreatment (8 weeks), ITT/LOCF (IG=26; CG=25), mean change (SD) IG: -8.65 (1.31) CG: -3.52 (1.06) Difference in mean change NR (95% CI, -8.57 to -1.70); p=0.005
		CGI-S, mean improvement in score, posttreatment (8 weeks), ITT (IG=26; CG=25) Significantly greater for IG compared with CG P<0.001
		CGI-S, mean score, posttreatment (8 weeks), ITT (IG=26; CG=25), mean (SD) IG: 2.8 (0.3) CG: 3.6 (0.2) p=0.032

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	IG1: Parent-delivered brief CBT (N=61) IG2: Parent-delivered full CBT (N=64) CG: Wait-list control (N=69)	SCAS-P, posttreatment (12 weeks), unclear (IG1=38; IG2=42; CG=46), mean (SD) IG1: 24.16 (12.93) IG2: 20.45 (11.52) CG: 24.15 (11.36) IG1 vs. CG difference in change from baseline NR; P=NS IG2 vs. CG difference in change from baseline NR; P=NS SCAS-C, posttreatment (12 weeks), unclear (IG1=40; IG2=47; CG=57), mean (SD) IG1: 30.00 (12.6) IG2: 28.47 (20.0) CG: 29.40 (16.28) IG1 vs. CG difference in change from baseline NR; P=NS IG2 vs. CG difference in change from baseline NR; P=NS IG2 vs. CG difference in change from baseline NR; P=NS CGI-I, improvement at posttreatment (12 weeks), unclear (IG1=46; CG=63), N (%) IG1: 25 (54)
Villabo et al, 2018 ¹⁵⁰ NR	IG1: Individual CBT (N=55) IG2: Group CBT (N=55) CG: Wait-list (N=55)	IG2: 38 (76) CG: 16 (25) IG1 vs. CG adjusted RR: 1.89 (95% CI, 1.16 to 3.09); p=0.011 IG2 vs. CG adjusted RR: 2.64 (95% CI, 1.70 to 4.11); P<0.0001 MASC-C, posttreatment (12 weeks), ITT (IG1=44, IG2=52, CG=51), mean (SE) IG1: 48.61 (1.48) IG2: 48.80 (1.65) CG: 51.95 (1.60) IG1 vs. CG: effect Size Hedge's g (95% CI): 0.28 (0.10 to 0.65), p=NS IG2 vs. CG: effect Size Hedge's g (95% CI): 0.26 (0.12 to 0.64), p=NS Means adjusted for age, gender, number of comorbid conditions, and baseline ADIS CSR for each target anxiety disorder MASC-P, posttreatment (12 weeks), ITT (IG1=44, IG2=52, CG=51), mean (SE) IG1: 47.25 (2.58) IG2: 49.72 (2.46) CG: 50.86 (2.45)
		IG1 vs. CG: effect Size Hedge's g (95% CI): 0.20 (0.18 to 0.61), p=NS IG2 vs. CG: effect Size Hedge's g (95% CI): 0.06 (-0.34 to 0.48), p=NS Means adjusted for age, gender, number of comorbid conditions, and baseline ADIS CSR for each target anxiety disorder

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Anxiety Symptoms
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30)	ADIS C/P change from baseline to 17 weeks, primary diagnosis, ITT (IG1=30; CG=30), N (%) IG1: 12 (40) CG: 7 (23.3)
	CG: Wait-list control (N=30)	OR=2.19 (95% CI, 0.72 to 6.70)
	(11-00)	ADIS C/P change from baseline to 17 weeks, remission of all ADs, ITT (IG1=30; CG=30), N (%) IG1: 8 (26.7) CG: 4 (13.3)
		OR=2.36 (95% CI, 0.63 to 8.92)
		CGI-I change from baseline to 17 weeks, ITT (IG1=30; CG=30), N (%) IG1: 12 (40)
		CG: 5 (16.7) OR=3.33 (95% CI, 1.00 to 11.14)
		CSR change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 3.89 (2.58) CG: 4.86 (2.19)
		ES=0.05 (95% CI, 0.00 to 0.19)
		SCAS-C change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 30.35 (19.17)
		CG: 33.46 (15.01) ES=0.05 (95% CI, 0.00 to 0.20)
		SCAS-P change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 33.12 (21.70)
		CG: 28.93 (15.79) ES=0.06 (95% CI, 0.00 to 0.21)
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶	IG1: Individual child- focused in-person CBT (N=139)	PARS change in score from baseline to 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) IG1: 10.8 (5.9) IG2: 9.8 (6.2)
Compton et al, 2014 ²⁰⁷	IG2: Sertraline	IG2. 9.8 (6.2)
Caporino et al, 2017 ²¹⁶	(N=133)	CG: 12.6 (6.3)
Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹	IG3: CBT + sertraline (N=140)	IG1 vs. CG: effect size Hedge's g (95% CI): 0.31 (0.02 to 0.59)
Gordon-Hollingsworth et	CG: Placebo (N=76)	IG2 vs. CG: effect size Hedge's g (95% CI): 0.45 (0.17 to 0.74) IG3 vs. CG: effect size Hedge's g (95% CI): 0.86 (0.56 to 1.15)
al, 2015 ²¹⁰		IG1 vs. CG: Time vs. Intervention: p=0.01
Ginsburg et al, 2011 ²¹¹		IG2 vs. CG: Time vs. Intervention: p=NS
NCT00052078		IG3 vs. CG: Time vs. Intervention: p=NS

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078 (continued)		CGI-S change in score from baseline to 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) IG1: 3.3 (1.3) IG2: 3.0 (1.3) IG3: 2.4 (1.3) CG: 3.8 (1.4) No statistics reported, CIs of individual treatments do not overlap MASC-C IG1: 40.9 (10.4) IG2: 38.2 (10.7) IG3: 39.5 (10.8) CG: 42.9 (11.8) IG2 vs. CG: b=-4.68, t=-2.80, adjusted p=0.03, all other comparisons not statistically significant, P=NR MASC-P IG1: 42.1 (16.1) IG2: 37.9 (17.3) IG3: 33.4 (16.9) CG: 49.1 (16.9) IG3 vs. CG: b=-7.0, t=-2.9, adjusted P<0.001 IG2 vs. CG: b=-11.1, t=-4.4, adjusted P<0.001 IG3 vs. CG: b=-15.7, t=-6.4, adjusted P<0.001
		SCARED-C IG1: 12.4 (11.4) IG2: 9.3 (11.9) IG3: 9.4 (11.6) CG: 13.8 (12.1) No statistically significant differences between arms, P=NR SCARED-P IG1: 16.9 (11.2) IG2: 11.0 (11.7) IG3: 9.6 (11.4) CG: 19.5 (11.8) IG1 vs. CG: adjusted p=0.26 IG2 vs. CG: b=-7.9, t=-4.7, adjusted P<0.001 IG3 vs. CG: b=-9.8, t=-5.9, adjusted P<0.001

Abbreviations: ADIS=Anxiety Disorders Interview Schedule; ADIS-C=Anxiety Disorders Interview Schedule for DSM-IV for Children-Children; ADIS-CSR=Anxiety Disorders Interview Schedule Clinician Severity Ratings; ADIS-DSM=Anxiety and Related Disorders Interview Schedule; ADIS-DSM-IV= Anxiety and Related Disorders Interview Schedule-Diagnostic and Statistical Manual-IV; CBT=cognitive behavioral therapy; CG=control group; CGI=Clinical Global Impressions; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; CSR=Clinician Severity Ratings; CSR-C=clinical rating scale-child-rated; CSR-P=clinical rating scale-parent rated; DISCAP=Diagnostic

Interview Schedule for Children, Adolescents, and Parents; ES=effect size; FSSCR=Fear Survey Schedule for Children-Revised; GAD=generalized anxiety disorder; HAM-D=HAM-D=Hamilton Depression Rating Scale; IG=intervention group; ITT=intent to treat; KQ=key question; LOCF=last observation carried forward; MASC=Multidimensional Anxiety Scale for Children; MASC=C=Multidimensional Anxiety Scale for Children-child; MASC-P= Multidimensional Anxiety Scale for Children-parent; mITT=modified intent to treat; NA=not available; NR=not reported; NS=not significant; OR=odds ratio; PARS=Pediatric Anxiety Rating Scale; PSCAS=Spence Children's Anxiety Scale-Parent; PSWQ-C=Penn State Worry Questionnaire for Children; RCMAS=Revised Children's Manifest Anxiety Scale RR=relative risk; SASC-R=Social Anxiety Scale for Children-Revised; SCARED-C=Screen for Anxiety Related Emotional Disorders-Parent; SCARED-R-C=Screen for Anxiety Related Emotional Disorders-Parent; SCARED-R-C=Screen for Anxiety Related Emotional Disorders-R-Children's Anxiety Scale; SCAS-C=Spence Children's Anxiety Scale-Child; SCAS-F=Spence Children's Anxiety Scale-Parent; SCAS-M=Spence Children's Anxiety Scale-Child-Mother; SCAS-P=Spence Children's Anxiety Scale-Parent; SD=standard deviation; SE=standard error; SepAD=separation anxiety disorder; SMQ-P=Selective Mutism Questionnaire-Parent; SocAD=social anxiety disorder; SPAI=Social Phobia and Anxiety Inventory; SPAI-C=Social Phobia and Anxiety Inventory for Parents; TAU=treatment as usual; WLC=waitlist control.

Author, Year, Registry	Treatment Interventions and	Downsonian Communication
Number	Comparators	Depression Symptoms
Arendt et al, 2016 ⁶⁵	IG1: Group child + parent in-person	S-MFQ youth, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD)
	CBT (N=56)	IG1: 2.96 (3.84)
	CG: Wait-list (N=53)	CG: 5.19 (5.32)
		Time-by-condition effect, p=0.020; partial eta squared=0.05
		S-MFQ mother, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD)
		IG1: 3.34 (3.78)
		CG: 5.79 (5.51)
		Time-by-condition effect, p=0.044; partial eta squared=0.04
		S-MFQ father, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD)
		IG1: 2.85 (4.03)
		CG: 5.73 (5.92)
		Time-by-condition effect, F=3.82; p=0.053; partial eta squared=0.04
Barrett et al, 1996 ⁷⁰	IG1: CBT (N=28)	CDI, posttreatment (12 weeks), completers (IG1=28; CG=23), mean (SD)
	IG2: CBT + family intervention	IG1: 4.5 (3.8)
	(N=25)	CG: 6.8 (5.3)
	CG: Wait-list (N=26)	Time x Treatment interaction=NS
		CDI, posttreatment (12 weeks), completers (IG2=25; CG=23), mean (SD)
		IG2: 4.1 (4.8)
		CG: 6.8 (5.3)
		Time x Treatment interaction=NS
Ishikawa et al, 2019 ¹⁰³	IG1: Individual child + parent in-	DSRS, posttreatment (2 or 4 months), completers (IG=25; CG=24), mean (SE)
	person CBT (N=26)	IG: 14.00 (1.54)
	CG: Wait-list (N=25)	CG: 16.50 (1.50)
		Time x Treatment interaction p=NS
		CDI, posttreatment (2 or 4 months), completers (IG=25; CG=24), mean (SE)
		IG: 14.64 (1.75)
		CG: 19.05 (1.86)
		Time x Treatment interaction P<0.05 favoring CBT

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Lyneham et al, 2006 ¹¹² NR	IG1: Parent-guided CBT supported by telephone (N=28) IG2: Parent-guided CBT supported by email (N=21) IG3: Parent-guided CBT with as needed support (N=29) CG: Wait-list (N=22)	CDI, pretreatment, ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 14.41 (9.79) IG2: 11.38 (3.79) IG3: 11.86 (9.75) CG: 10.33 (8.75) CDI, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), mean (SD) IG1: 7.44 (7.99) IG2: 9.24 (3.86) IG3: 8.62 (9.95) CG: 10.48 (8.44)
Ost et al, 2015 ¹²⁰	IG1: Individual + group child (N=16) IG2: Child + parent in-person CBT (N=16) CG: Wait-list (N=23)	Change in CDI from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD) IG1: 6.4 (6.1) IG: 9.3 (9.7) CG: 11.0 (7.7) Time x Treatment: F=1.2, p=NS
Perrin et al, 2019 ¹²² ISRCTN50951795	IG1: Individual child + parent in- person + internet CBT (N=20) CG: Wait-list control (N=20)	MFQ-P, posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD) IG1: 10.1 (9.7) CG: 20.9 (14.9) Effect size partial eta squared=0.19 P<0.01 MFQ-C, posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD) IG1: 6.9 (9.8) CG: 25.4 (14.4) Effect size partial eta squared=0.40 P<0.001
Rynn et al, 2001 ¹³⁰	IG1: Sertraline (N=11) CG: Placebo (N=11)	HAM-D, posttreatment (week 9), ITT (IG=11; CG=11), mean (SD) IG: 4.0 (3.6) CG: 11.5 (4.2) P<0.001

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	IG1: Individual child-focused internet CBT (N=35) CG: Wait-list control group (N=35)	S-MFQ-C, change from baseline to posttreatment (14 weeks), ITT (IG1=35, CG=35), between-group change effect size Cohen's d=0.11; p=0.932
		S-MFQ-M, change from baseline to posttreatment (14 weeks), ITT (IG1=35, CG=35), between-group change effect size Cohen's d=0.60; p=0.008
		S-MFQ-F, change from baseline to posttreatment (14 weeks), ITT (IG1=35, CG=35), between-group change effect size Cohen's d=0.07; p=0.813
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	IG1: Parent-delivered brief CBT (N=61) IG2: Parent-delivered full CBT (N=64) CG: Wait-list control (N=69)	SMFQ-P, posttreatment (12 weeks), unclear (IG1=39; IG2=43; CG=49), mean (SD) IG1: 4.54 (5.19) IG2: 2.00 (2.77) CG: 4.86 (5.28) IG1 vs. CG difference in change from baseline: NR IG2 vs. CG difference in change from baseline: -1.44 (95% CI, -2.82 to -0.07), p=0.0395
		SMFQ-C, posttreatment (12 weeks), unclear (IG1=42; IG2=48; CG=57), mean (SD) IG1: 5.57 (5.06) IG2: 3.94 (5.04) CG: 4.84 (5.38) IG1 vs. CG difference in change from baseline: NR IG2 vs. CG difference in change from baseline: NR
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30) CG: Wait-list control (N=30)	Short MFQ-C change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 6.48 (6.4) CG: 7.70 (7.05) ES=0.00 (95% CI, 0.00 to 0.10)
		Short MFQ-P change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 6.73 (6.91) CG: 7.11 (7.44) ES=0.00 (95% CI, 0.00 to 0.07)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	IG1: Individual child-focused inperson CBT (N=139) IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	MFQ-Youth, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) IG1: 5.3 (7.9) IG2: 4.6 (8.3) IG3: 4.8 (8.1) CG: 6.4 (8.5) No statistically significant differences between arms, P=NR MFQ-P, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) IG1: 8.1 (7.1) IG2: 5.0 (7.4) IG3: 4.1 (7.2) CG: 8.0 (7.5) IG1 vs. CG: adjusted p=0.91 IG2 vs. CG: b=-3.0, t=-2.8, adjusted P<0.001 IG3 vs. CG: b=-3.9, t=-3.7, adjusted P<0.001

Abbreviations: CBT=cognitive behavioral therapy; CDI=Children's Depression Inventory; CG=control group; CI=confidence interval; DSRS=Depression Self-Rating Scale; ES=effect size; HAM-D=Hamilton Depression Rating Scale; IG=intervention group; ITT=intent to treat; KQ=key question; MFQ=Mood & Feelings Questionnaire; MFQ-C=Mood and Feelings Questionnaire for Children; MFQ-P=Mood and Feelings Questionnaire for Parents; NR=not reported; NS=not significant; SD=standard deviation; SE=standard error; S-MFQ=Short Mood and Feelings Questionnaire for Parents; S-MFQ-C= Mood and Feelings Questionnaire-Fathers; S-MFQ-M= Mood and Feelings Questionnaire-Mothers.

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Arendt et al, 2016 ⁶⁵	IG1: Group child + parent in-person CBT (N=56) CG: Wait-list (N=53)	Response Clinically significant change based on SCAS-Child using method of Jacobson and Truax Clinically significant change based on SCAS-Mother using method of Jacobson and Truax Clinically significant change based on SCAS-Father using method of Jacobson and Truax Clinically significant change based on SCAS-Father using method of Jacobson and Truax Clinically significant change based on SCAS-Child, posttreatment (10 weeks), ITT (IG1=56; CG=53), N (%) IG1: 24 (42.9) CG: 6 (11.3) P<0.001 Clinically significant change based on SCAS-Mother, posttreatment (10 weeks), ITT (IG1=56; CG=53), N (%) IG1: 29 (51.8) CG: 6 (11.3) P<0.001 Clinically significant change based on SCAS-Father, posttreatment (10 weeks), ITT (IG1=56; CG=53), N (%) IG1: 23 (41.8)
		CG: 5 (9.8) P<0.001 Loss of Diagnosis Free of primary diagnosis (ADIS) Free of all anxiety diagnoses (ADIS) Free of primary diagnosis, posttreatment (10 weeks), ITT (IG1=56; CG=53), N (%) IG1: 37 (66.1) CG: 4 (7.5) P<0.001 Free of all anxiety diagnoses, posttreatment (10 weeks), ITT (IG1=56; CG=53), N (%) IG1: 27 (48.2) CG: 3 (5.7) P<0.001
Barrett et al, 1996 ⁷⁰	IG1: CBT (N=28) IG2: CBT + family intervention (N=25) CG: Wait-list (N=26)	Loss of Diagnosis No longer meeting DSM-III-R criteria for a current anxiety disorder No longer meeting DSM-III-R criteria for a current anxiety disorder, posttreatment (12 weeks), completers (IG1/2=53, CG=23), N (%) IG1/2: 37 (69.8) CG: 6 (26.0) P<0.05
Birmaher et al, 2003 ⁷³	IG1: Fluoxetine (N=37) CG: Placebo (N=37)	Response CGI-I ≤2 at end of treatment (12 weeks) CGI-I ≤2, posttreatment (12 weeks), mITT (IG1=36, CG=37), N% IG1: 22 (61) CG: 13 (35) p=0.03, ES=0.26

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Black et al, 1994 ⁷⁴	IG1: Fluoxetine (N=6) CG: Placebo (N=9)	Response CGI response (markedly or much improved vs. minimally improved, no change, or worse) with respect to mutism CGI mutism parent rated marked or much improved, posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%) IG1: 4 (66.7) CG: 1 (11.1) p=0.03 CGI mutism clinician rated marked or much improved, posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%) IG1: 3 (50) CG: 4 (44.4) p=NS
Cobham et al, 2017 ⁷⁷	IG1: Group parent-only in-	CGI mutism teacher rated marked or much improved; posttreatment (12 weeks), ITT (IG1=6; CG=9), N (%) IG1: 4 (66.6) CG: 4 (44.4) p=NS Loss of Diagnosis
ACTRN126150005145 05	person CBT (N=33) CG: Wait-list control (N=30)	Absence of any anxiety diagnosis based on diagnostic interview (ADIS) ADIS, absence of any anxiety diagnosis, posttreatment (6 weeks), mITT (IG1=31, CG=29), N% IG1: 12 (38.7) CG: 1 (3.4) P<0.001 RR (95% CI): 0.56 (0.47 to 0.82) ADIS, absence of primary anxiety diagnosis, posttreatment (6 weeks), mITT (IG1=31, CG=29), N% IG1: 20 (64.5)
		CG: 5 (16.2) P<0.001 RR (95% CI): 0.43 (0.259 to 0.709)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Cornacchio et al, 2019 ⁷⁹ NA	IG1: Group child + parent in-person CBT (N=14) CG: Wait-list control (N=15)	Response CGI-I score of 1 ("very much improved") or 2 ("much improved") CGI-I ≤2, posttreatment (4 weeks), ITT (IG1=14; CG=15), N (%) IG1: 7 (50) CG: 0 (0) Fisher's p=0.006 Effect size phi=-0.58
		Loss of Diagnosis Loss of selective mutism diagnosis based on ADIS/C-P Loss of selective mutism diagnosis ADIS C/P, 4 weeks, ITT (IG1=14; CG=15), N (%) IG1: 1 (7.1) CG: 0 (0) Fisher's p=1.00 Effect size phi=0.19
Donovan et al, 2014 ⁸³ ACTRN126120001398 75	IG1: Individual parent- focused internet CBT (N=23) CG: Wait-list (N=29)	Loss of Diagnosis Absence of primary anxiety diagnosis, absence of any anxiety diagnosis (ADIS) Absence of primary diagnosis, posttreatment (8 weeks), mITT (IG1=23, CG=27), N (%) IG1: 9 (39.1) CG: 7 (25.9) p=0.318 Absence of any diagnosis, posttreatment (8 weeks), mITT (IG1=23, CG=27), N (%) IG1: 8 (34.8) CG: 7 (25.9) p=0.496

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Ginsburg et al, 2020 ⁹²	IG1: Individual child- focused in-person CBT (N=148) CG: TAU (N=68)	Response Responder (receiving a CGI-I score of 1 or 2) Responder, posttreatment (12 weeks), ITT (IG=148; CG=68), N (%) IG: NR (42.1) CG: NR (36.7) p=0.34 Responder, 12 months, ITT (IG=148; CG=68), N (%) IG: NR (47.7)
		CG: NR (57.1) p=0.24 Loss of Diagnosis No anxiety disorder (loss of all study entry anxiety diagnosis) using ADIS Loss of primary anxiety disorder using ADIS No anxiety disorder, posttreatment (12 weeks), ITT (IG=148; CG=68), N (%) IG: NR (34.9) CG: NR (35.0) p=0.67
		No anxiety disorder, 12 months, ITT (IG=148; CG=68), N (%) IG: NR (48.6) CG: NR (53.1) p=0.69 Loss of primary anxiety disorder, posttreatment (12 weeks), ITT (IG=148; CG=68), N (%) IG: NR (40.5)
		CG: NR (43.3) p=0.61 Loss of primary anxiety disorder, 12 months, ITT (IG=148; CG=68), N (%) IG: NR (53.2) CG: NR (59.2) p=0.44

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Hirshfeld-Becker et al, 2010 ⁹⁸	IG1: Individual child + parent in-person CBT (N=34) CG: Wait-list control (N=30)	Response CGI-I ≤2 (much improved or very much improved) CGI-I score ≤2, posttreatment (6 months), ITT (IG1=34; CG=30), n (%) IG1: 20 (59) CG: 9 (30) p=0.016 NNT 3.5 (95% CI NR)
		Loss of Diagnosis Absence of anxiety diagnosis based on clinical interview Absence of anxiety diagnosis, posttreatment (6 months), ITT (G1=34; CG=30), n (%) IG1: 17 (50) CG: 5 (17) P<0.01
Holmes et al, 2014 ⁹⁹ ACTRN126120000618 31	IG1: Group child-focused in-person CBT (N=20) CG: Wait-list control (N=22)	Loss of Diagnosis No longer meeting criteria for diagnosis (any anxiety, GAD) ADIS-C/P absence of GAD diagnosis, posttreatment (10 weeks), ITT (IG1=20, CG=22), % IG1: 45 CG: 0 P<0.001
		ADIS-C/P absence of GAD diagnosis, posttreatment (10 weeks), completers (IG1=17, CG=19), % IG1: 52.9 CG: 0 P<0.001
		ADIS-C/P absence of any anxiety diagnosis, posttreatment (10 weeks), ITT (IG1=20, CG=22), % IG1: 15 CG: 0 p=0.059
		ADIS-C/P absence of any anxiety diagnosis, posttreatment (10 weeks), completers (IG1=17, CG=19), % IG1: 17.6 CG: 0 p=0.056

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Ishikawa et al, 2019 ¹⁰³	IG1: Individual child + parent in-person CBT (N=26) CG: Wait-list (N=25)	Response A clinically significant change was examined based on a Reliable Change Index (RCI) and a nondysfunctional range. The RCI was calculated based on standard errors of pretreatment scores. When the RCI was greater than 1.96, the children were considered to show clinically meaningful change. Clinical cutoff points were applied to set a non-dysfunctional range when obtained Proportion of participants showing clinical significance change, SCAS-C Proportion of participants showing clinical significance change, DSRS Proportion of participants showing clinical significance change, CDI Proportion of participants showing clinical significance change, SCAS-P Proportion of participants showing clinical significance change in SCAS-C, posttreatment (2 or 4 months), completer (IG=25; CG=24), N (%) IG: 14 (56.0) CG: 9 (37.5) p=0.20
		Proportion of participants showing clinical significance change in DSRS, posttreatment (2 or 4 months), completer (IG=25; CG=24), N (%) IG: 9 (36.0) CG: 5 (20.83) p=0.24
		Proportion of participants showing clinical significance change in CDI, posttreatment (2 or 4 months), completer (IG=25; CG=24), N (%) IG: 10 (40.0) CG: 4 (16.67) p=0.07
		Proportion of participants showing clinical significance change in SCAS-P, posttreatment (2 or 4 months), completer (IG=25; CG=24), N (%) IG: 8 (32.0) CG: 5 (20.83) p=0.38
		Remission Proportion free of principal diagnosis, posttreatment (2 or 4 months), ITT (IG=26; CG=25), N (%) IG: 13 (50.0) CG: 3 (12.0) P<0.01
		Proportion free of any diagnosis, posttreatment (2 or 4 months), ITT (IG=26; CG=25), N (%) IG: 4 (15.38) CG: 1 (4.0) p=NS

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Lau et al, 2010 ¹¹⁰ NR	IG1: Group child + parent in-person CBT (N=26) CG: Wait-list control (N=25)	Loss of Diagnosis K-SADS anxiety diagnostic status Presence of anxiety diagnosis of symptoms, posttreatment (13 weeks), mITT (IG1=24; CG=21), N (%) IG1: 16 (67) CG: 21 (100) P<0.01
		Absence of anxiety diagnosis or subclinical symptoms, posttreatment (13 weeks), mITT (IG1=24; CG=21), N (%) IG1: 8 (33) CG: 0 (0)
Lyneham et al, 2006 ¹¹² NR	IG1: Parent-guided CBT supported by telephone (N=28) IG2: Parent-guided CBT supported by email (N=21) IG3: Parent-guided CBT with as needed support (N=29) CG: Wait-list (N=22)	Remission Return to normal range for SCAS-C (overall or for any subscales) SCAS-C normal range, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22), % IG1: 62 IG2: 57 IG3: 50 CG: 23 Any IG: 57 Any IG vs. CG: P<0.05 Loss of Diagnosis ADIS, no longer met criteria for principal anxiety disorder and/or any anxiety disorder ADIS loss of principal anxiety disorder, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22) Any IG vs. CG, P<0.01 ADIS loss of any anxiety disorder, posttreatment (12 weeks), ITT (IG1=28, IG2=21, IG3=29, CG=22) Any IG vs. CG, P<0.01
Ost et al, 2015 ¹²⁰	IG1: Individual + group child (N=16) IG2: Child + parent in- person CBT (N=16) CG: Wait-list (N=23)	Loss of Diagnosis No longer fulfilling criteria for social phobia (ADIS) ADIS absence of social phobia (12 months), ITT (IG1=16; IG2=16; CG=23), N (%) IG1: 9 (56) IG2: 10 (62) CG: 2 (9) IG1 vs. CG: p≤0.001, favoring IG1 IG2 vs. CG: p≤0.001, favoring IG2

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Perrin et al, 2019 ¹²² ISRCTN50951795	IG1: Individual child + parent in-person + internet CBT (N=20) CG: Wait-list control (N=20)	Loss of Diagnosis Presence of GAD based on ADIS Presence of comorbid disorders based on ADIS Recovery from all disorders based on ADIS ADIS GAD diagnosis present, posttreatment (10 weeks), ITT (IG1=20, CG=20), N (%) IG1: 4 (20) CG: 20 (100) p<0.001 ADIS comorbid disorder diagnosis present, posttreatment (10 weeks), ITT (IG1=20, CG=20), N (%) IG1: 1 (5)
Pine et al. 2001 ¹²⁴	IG1: Fluvoxamine (N=63)	CG: 11 (55) p<0.001 ADIS recovery from all disorders, posttreatment (10 weeks), ITT (IG1=20, CG=20), N (%) IG1: 16 (80) CG: 0 (0) p<0.000 Response
Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵	IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=65)	Response to treatment defined as CGI-I <4 CGI-I score <4, posttreatment (8 weeks), ITT (IG1=63: CG=65), N (%) IG1: 48 (76) CG: 19 (29) P<0.001
Rudy et al, 2017 ¹²⁹ NCT02051192	IG1: Individual parent-led in-person CBT (N=12) CG: TAU (N=10)	Response CGI-I scores of much improved or very much improved CGI-I much improved/very much improved, 5 weeks, ITT (IG1=12; CG=10), N% IG1: 10 (83.3) CG: 0 (0.0) P<0.001
		Remission ADIS-CSR scores <4 ADIS CSR <4, 5 weeks, ITT (IG1=12; CG=10), N% IG1: 8 (66.7) CG: 1 (10.0) p=0.011

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Rynn et al, 2001 ¹³⁰	IG1: Sertraline (N=11) CG: Placebo (N=11)	Response Moderately or markedly improved (CGI-I scale scores=1 or 2) CGI-I=1 or 2, posttreatment (week 9), ITT (IG=11; CG=11), N (%) IG: 10 (91) CG: 1 (9) P<0.001
		Remission Remission rate "markedly improved" based on CGI=1 CGI=1, posttreatment (week 9), ITT (IG=11; CG=11), N (%)
		IG: 2 (18) CG: 0 (0)
Salzer et al, 2018 ^{42,} ISRCTN 22752528	IG1: Individual child- focused in-person CBT (N=34) CG: Wait-list control (N=39)	Response LSAS-CA ≥31% reduction in total score LSAS-CA response, posttreatment, ITT (IG1=34; CG=39), N (%) IG1: NR (66) CG: NR (20) OR: 7.91 (95% CI, 2.17 to 28.86); p=0.0056
		Remission LSAS-CA total score ≤30 LSAS-CA remission, posttreatment, mITT (IG1=32; CG=36), N (%) IG1: 47 CG: 6 OR: 14.6 (95% CI, 1.85 to 114.95); p=0.0009
Shortt et al, 2001 ¹³⁴	IG1: Group child + parent in-person CBT (N=54) CG: Wait-list (N=17)	Loss of Diagnosis Anxiety-free diagnosis based on clinical interview with parent Anxiety-free diagnosis, 10 weeks, ITT (IG1=54, CG=17), N (%) IG1: NR CG: NR IG1 vs. CG: P<0.001 Anxiety-free diagnosis, 10 weeks, completers (IG1=48, CG=16), N (%) IG1: 33 (69) CG: 1 (6) P<0.001

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	IG1: Individual child- focused internet CBT (N=35) CG: Wait-list control group (N=35)	Response Improved SCAS scores that were statistically reliable according to the reliable change index 14 weeks Improved by SCAS-C, at posttreatment (14 weeks), (IG1=32; CG=31), N (%) IG1: 22 (69) CG: 8 (26) p=0.001 Improved by SCAS-M scores, at posttreatment (14 weeks), (IG1=35; CG=32), N (%) IG1: 24 (69) CG: 7 (22) P<0.001 Improved by SCAS-F scores, at posttreatment (14 weeks), (IG1=25; CG=27), N (%) IG1: 9 (35) CG: 5 (19) p=0.156
		Remission SCAS scores that were statistically reliable according to the reliable change index and were deemed a clinical change were considered recovered, but specific score thresholds not reported. Recovered by SCAS-C, at posttreatment (14 weeks), mITT (IG1=32; CG=31), N (%) IG1: 14 (44) CG: 2 (6) p=0.001 Recovered by SCAS-M, at posttreatment (14 weeks), mITT (IG1=35; CG=32), N (%) IG1: 9 (26) CG: 2 (6) p=0.032 Recovered by SCAS-F, at posttreatment (14 weeks), mITT (IG1=25; CG=27), N (%) IG1: 1 (4) CG: 2 (7) p=1.00
		Loss of Diagnosis Free of diagnosis based on ADIS-IV Free of primary anxiety diagnosis, at posttreatment (14 weeks), mITT (IG1=35; CG=32), N (%) IG1: 14 (40) CG: 5 (16) OR: 3.6 (95% CI NR); p=0.027 Free of any anxiety diagnosis, at posttreatment (14 weeks), mITT (IG1=35; CG=32), N (%) IG1=10 (29) CG: 1 (3) OR: 12.4 (95% CI NR); p=0.005

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Strawn et al, 2015 ¹⁴² NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	Response Response: 50% improvement on PARS severity for GAD 50% improvement on PARS severity for GAD, post acute treatment (10 weeks), ITT (IG=135; CG=133), % IG: 59 CG: 42 P≤0.05, favoring duloxetine
		Remission: CGI-Severity ≤2 Remission: PARS severity for GAD ≤8 CGI-Severity ≤2, post acute treatment (10 weeks), ITT (IG=135; CG=133), % IG: 54 CG: 35 P≤0.01, favoring duloxetine PARS severity for GAD ≤8, post acute treatment (10 weeks), ITT (IG=135; CG=133), % IG: 50 CG: 34 P≤0.05, favoring duloxetine
Strawn et al, 2020 ¹⁴³ NCT02818751	IG1: Escitalopram (N=26) CG: Placebo (N=25)	Response CGI-I score ≤2, posttreatment (8 weeks), ITT/LOCF (IG=26; CG=25), N (%) IG: 16 (62) CG: 6 (24) RR: NR (95% CI, 0.578 to 0.95); p=0.0039
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	IG1: Parent-delivered brief CBT (N=61) IG2: Parent-delivered full CBT (N=64) CG: Wait-list control (N=69)	Loss of Diagnosis Loss of diagnosis based on ADIS ADIS loss of primary diagnosis, 12 weeks, unclear (IG1=46; IG2=50; CG=63), N (%) IG1: 18 (39) IG2: 25 (50) CG: 16 (25) IG1 vs. CG adjusted RR: 1.56 (0.89 to 2.74); p=0.119 IG2 vs. CG adjusted RR: 1.85 (1.14 to 2.99); p=0.013 ADIS loss of any diagnosis, 12 weeks, unclear (IG1=46; IG2=50; CG=63) N (%) IG1: 7 (15) IG2: 17 (34) CG: 7 (11) IG1 vs. CG adjusted RR: 1.47 (0.56 to 3.88); p=0.433 IG2 vs. CG adjusted RR: 3.13 (1.40 to 7.01); p=0.006

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Villabo et al, 2018 ¹⁵⁰ NR	IG1: Individual CBT (N=55) IG2: Group CBT (N=55) CG: Wait-list (N=55)	Loss of Diagnosis Loss of all anxiety disorders based on ADIS, loss of primary anxiety diagnosis based on ADIS ADIS loss all anxiety diagnosis, posttreatment (12 weeks), ITT (IG1=44, IG2=52 CG=51), % (95% CI) IG1: 38 (24 to 52) IG2: 56 (43 to 69) CG: 6 (-1 to 0.14) IG1 vs. CG: ARD 31 (16 to 47), P<0.001 IG2 vs. CG: ARD 50 (34 to 65), P<0.001 ADIS loss primary anxiety diagnosis, posttreatment (12 weeks), ITT (IG1=44, IG2=52 CG=51), % (95% CI) IG1: 52 (38 to 67) IG2: 65 (52 to 78) CG: 14 (4 to 23) IG1 vs. CG: ARD 38 (21 to 56), P<0.001 IG2 vs. CG: ARD 51 (35 to 68), P<0.001
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30) CG: Wait-list control (N=30)	Response Clinical improvement: CGI-I ≤2 CGI-I ≤2, baseline to 17 weeks, ITT (IG1=30; CG=30), N (%) IG1: 12 (40.0) CG: 9 (30.0) OR=1.56 (95% CI, 0.53 to 4.53) Loss of Diagnosis Loss of AD diagnosis based on ADIS Loss of AD diagnosis, 17 weeks, ITT (IG1=30; CG=30), N (%) ADIS C/P Remission of primary AD: IG1: 12 (40) CG: 7 (23.3) OR=2.19 (95% CI, 0.72 to 6.70) Remission of all ADs IG1: 8 (26.7) CG: 4 (13.3) OR=2.36 (95% CI, 0.63 to 8.92)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	IG1: Individual child- focused in-person CBT (N=139) IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	Response Response score on CGI-I ≤2 CGI-I ≤2, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 83 (59.7) IG2: 73 (54.9) IG3: 113 (80.7) CG: 18 (23.7) IG1 vs. CG: OR: 4.8 (95% CI, 2.6 to 9.0), P<0.001 IG2 vs. CG: OR: 3.9 (95% CI, 3.0 to 5.9), P<0.001 IG3 vs. CG: OR: 13.6 (95% CI, 6.9 to 26.8), P<0.001 Numbers needed to treat, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), N (CI) IG1 vs. CG: 2.8 (2.7 to 3.0) IG2 vs. CG: 3.2 (3.2 to 3.5) IG3 vs. CG: 1.7 (1.7 to 1.9)
		Remission 1. CGI-S score ≤2 2. CGI-I score=1 CGI-S ≤2, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 50 (35.9) IG2: 62 (46.3) IG3: 91 (64.9) CG: 21 (27.1) IG1 vs. CG: OR: 1.65 (0 to 3.53), p=0.49 IG2 vs. CG: OR: 2.55 (0 to 5.48), p=0.29 IG3 vs. CG: OR: 5.59 (0 to 12.07), p=0.16 CGI-I=1, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 28 (20.4) IG2: 45 (33.9) IG3: 64 (45.6) CG: 11 (15.0) IG1 vs. CG: OR: 1.77 (0 to 4.78), p=0.61 IG2 vs. CG: OR: 3.56 (0 to 9.53), p=0.39

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Walkup et al, 2008 ¹⁵³	una comparators	Loss of Diagnosis
Albano et al, 2018 ²⁰⁵ ;		Loss of anxiety diagnosis (AD) using clinical interview
Taylor et al 2018 ²⁰⁶ ;		Loss of ADs at 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), N (%)
Compton et al,		IG1: 64 (46.2)
2014 ²⁰⁷ ;		IG2: 61 (45.9)
Caporino et al,		IG3: 96 (68.3)
2017 ²¹⁶ ; Sachez et al,		CG: 18 (23.7)
2019 ²⁰⁸ ; Rynn et al,		IG1 vs. CG: OR: 2.91 (1.03 to 4.79), p=0.05
2015 ²⁰⁹ ; Gordon-		IG2 vs. CG: OR: 2.84 (1.01 to 4.67), p=0.05
Hollingsworth et al,		IG3 vs. CG: OR: 7.47 (2.63 to 12.64), p=0.01
2015 ²¹⁰ ;		
Ginsburg et al, 2011 ²¹¹		
NCT00052078		
(continued)		

Abbreviations: ADIS=Anxiety and Related Disorders Interview Schedule for DSM-IV -Children; ADIS-CSR=Anxiety and Related Disorders Interview Schedule for DSM-IV -Children; ADIS-CSR=Anxiety and Related Disorders Interview Schedule IV; ARD=absolute risk difference; CBT=cognitive behavioral therapy; CDI=Children's Depression Inventory; CG=control group; CGI=Clinical Global Impressions; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; CSR=Clinician Severity Ratings; DSM-III-R=Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition-Revised; DSRS=Depression Self-Rating Scale; ES=effect size; G=group; GAD=generalized anxiety disorder; IG=intervention group; ITT=intent to treat; KQ=key question; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children; LOCF=last observation carried forward; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; mITT=modified intent to treat; NA=not available; NNT=number needed to treat; NR=not reported; NS=not significant; OR=odds ratio; PARS=Pediatric Anxiety Rating Scale; RCI=Reliable Change Index; RR=relative risk; SCAS=Spence Children's Anxiety Scale; SCAS-C=Spence Children's Anxiety Scale-Child-rated; SCAS-F=Spence Children's Anxiety Scale-Father; SCAS-M=Spence Children's Anxiety Scale-Mother-rated; SCAS-P=Spence Children's Anxiety Scale-Parent-rated; TAU=treatment as usual.

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes
Arendt et al, 2016 ⁶⁵	IG1: Group child + parent inperson CBT (N=56) CG: Wait-list (N=53)	CALIS youth, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 7.55 (6.46) CG: 10.94 (7.20) Time-by-condition effect, p=0.008, partial eta squared=0.06 CALIS mother, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 10.61 (7.28) CG: 17.94 (9.07) Time-by-condition effect, P<0.001, partial eta squared=0.14 CALIS father, posttreatment (10 weeks), ITT (IG1: 56; CG: 53), mean (SD) IG1: 10.96 (7.72) CG: 17.14 (9.16) Time-by-condition effect, F=12.45, P<0.001, partial eta squared=0.11	
Asbrand et al, 2020 ⁶⁷ TU 78/5-2, HE 3342/4-2	IG1: Group child-focused in- person CBT (N=31) CG: Wait-list control (N=36)	NR	Severity of diagnosis, posttreatment (12 weeks), ITT (IG1=31; CG=36), group effect, F(1)=7.24, p=0.007, Time x Group interaction F(1)=16.23, p <0.001 favoring CBT No subgroups of interest reported
Birmaher et al, 2003 ⁷³	IG1: Fluoxetine (N=37) CG: Placebo (N=37)	CGAS, posttreatment (12 weeks), ITT (IG1=37, CG=37), mean (SD) IG1: 70.3 (15.0) CG: 61.2 (10.9) Treatment x Time baseline to 12 weeks p=0.0001 CGAS ≥70, posttreatment (12 weeks), ITT (IG1=37, CG=37), N (%) IG1: 15 (40.5) CG: 10 (27.0) p=0.20; ES=0.14	NR
Cornacchio et al, 2019 ⁷⁹ NA	IG1: Group child + parent in- person CBT (N=14) CG: Wait-list control (N=15)	CGAS, posttreatment (4 weeks), ITT (IG1=14; CG=15), mean (SD) IG1: 53.6 (4.6) CG: 52.5 (4.9) P<0.01 Effect size Cohen's d=0.73	NR

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes
Donovan et al, 2014 ⁸³ ACTRN12612000139875	IG1: Individual parent- focused internet CBT (N=23) CG: Wait-list (N=29)	CGAS, posttreatment (8 weeks), mITT (IG1=23; CG=27), mean (SD) IG1: 66.91 (10.63) CG: 61.85 (9.98) Time x Treatment p=0.016, partial eta squared=0.115 For ITT population: Time x Treatment p=0.010, partial eta squared=0.125	NR
Ginsburg et al, 2020 ⁹²	IG1: Individual child-focused in-person CBT (N=148) CG: TAU (N=68)	CGAS, posttreatment (12 weeks), ITT (IG=148; CG=68), mean IG: 55.98 CG: 54.22 p=0.42 CGAS, 12 months, ITT (IG=148; CG=68), mean IG: 58.92 CG: 59.22 p=0.63	NR
Holmes et al, 2014 ⁹⁹ ACTRN12612000061831	IG1: Group child-focused in- person CBT (N=20) CG: Wait-list control (N=22)	CGAS, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 63.82 (11.03) CG: 51.05 (7.66) p=0.02; partial eta squared=0.15 Pediatric QOL Inventory-C, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 76.09 (15.17) CG: 66.88 (12.03) Time x Group interaction p=NS Pediatric QOL Inventory-P, posttreatment (10 weeks), completers (IG1=17, CG=19), mean (SD) IG1: 79.17 (14.16) CG: 75.34 (11.74) Time x Group interaction p=NS	NR
Ost et al, 2015 ¹²⁰	IG1: Individual + group child (N=16) IG2: Child + parent in-person CBT (N=16) CG: Wait-list (N=23)	Change in QOLI-C from baseline to posttreatment (12 weeks), ITT (IG1=16; IG2=16; CG=23), mean (SD) IG1: 3.85 (1.84) IG2: 3.46 (1.63) CG: 2.89 (1.40) Time x Treatment: F=4.1, P<0.05 IG1 vs. CG: p=NS IG2 vs. CG: p=NS	NR

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes
Perrin et al, 2019 ¹²² ISRCTN50951795	IG1: Individual child + parent in-person + internet CBT (N=20) CG: Wait-list control (N=20)	CGAS, posttreatment (10 weeks), ITT (IG1=20, CG=20), mean (SD) IG1: 82.1 (8.9) CG: 59.4 (6.7) Effect size partial eta squared=0.70 p<0.001	NR
		PQ-LES-Q, posttreatment 10 weeks), ITT (IG1=20, CG=20), mean (SD) IG1: 60.8 (10.7) CG: 48.7 (9.4) Effect size partial eta squared=0.23 P<0.01	
Thirlwall et al, 2013 ¹⁴⁵ ISRCTN92977593	IG1: Parent-delivered brief CBT (N=61) IG2: Parent-delivered full CBT (N=64) CG: Wait-list control (N=69)	CAIS-P, posttreatment (12 weeks), unclear (IG1=39; IG2=41; CG=48), mean (SD) IG1: 13.97 (14.64) IG2: 6.39 (6.29) CG: 15.56 (12.31) IG1 vs. CG difference in change from baseline NR, P=NS IG2 vs. CG difference in change from baseline, -5.56 (95% CI, -9.40 to -1.73), p=0.0045	NR
Salzer et al, 2018 ⁴² . ISRCTN 22752528	IG1: Individual child-focused in-person CBT (N=34) CG: Wait-list control (N=39)	NR	LSAS-CA deterioration, posttreatment, ITT (IG1=34; CG=39), N (%) IG1: NR (9.4) CG: NR (11.3)
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	IG1: Individual child-focused internet CBT (N=35) CG: Wait-list control group (N=35)	WHO-5, change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.04; p=0.945 CALIS-C change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.21; p=0.254 CALIS-M change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.93; P<0.001 CALIS-F change in score from baseline to posttreatment (14 weeks), ITT (IG1=35; CG=35), between-group effect size Cohen's d=0.20; p=0.227	NR

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes
Strawn et al, 2015 ¹⁴² NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	CGAS mean change from baseline to post acute treatment (10 weeks), ITT (IG=135; CG=133), mean (SE) IG: 17.1 (1.2) CG: 12.2 (1.2) P≤0.01, favoring duloxetine CGAS >70 (functional remission), post acute treatment (10 weeks),	NR
		ITT (IG=135; CG=133), % IG: 59 CG: 42 P≤0.05, favoring duloxetine	
Villabo et al, 2018 ¹⁵⁰ NR	IG1: Individual CBT (N=55) IG2: Group CBT (N=55) CG: Wait-list (N=55)	CGAS, posttreatment (12 weeks), ITT (IG1=44, IG2=52, CG=51), mean (SE) IG1: 62.52 (1.17) IG2: 62.81 (1.10) CG: 53.05 (1.09) IG1 vs. CG: effect size Hedge's g (95% CI): 1.01 (0.68 to 1.35), P<0.001 IG2 vs. CG: effect size Hedge's g (95% CI): 1.04 (0.72 to 1.37)	NR
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30) CG: Wait-list control (N=30)	CGAS change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 59.48 (14.87) CG: 55.18 (12.48) ES: 0.04 (95% CI, 0.00 to 0.18) CAIS-C change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 18.04 (16.97) CG: 17.59 (13.09) ES=0.01 (95% CI, 0.00 to 0.12) CAIS-P change from baseline to 17 weeks, ITT (IG1=30; CG=30),	CGI-I change from baseline to 17 weeks, ITT (IG1=30; CG=30), N (%) IG1: 12 (40) CG: 5 (16.7) OR=3.33 (95% CI, 1.00 to 11.14) Short MFQ-C change from baseline to 17 weeks, ITT (IG1=30; CG=30), mean (SD); effect size (95% CI) IG1: 6.48 (6.4)
		mean (SD); effect size (95% CI) IG1: 23.60 (21.81) CG: 19.63 (16.34) ES=0.04 (95% CI, 0.00 to 0.19)	CG: 7.70 (7.44) ES=0.00 (95% CI, 0.00 to 0.07)

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	IG1: Individual child-focused in-person CBT (N=139) IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	CGAS, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) IG1: 63.8 (10.2) IG2: 65.0 (10.7) IG3: 68.6 (10.4) CG: 60.1 (10.9) No statistics reported, all active treatments noted to be superior to placebo CAIS-C IG1: 9.1 (10.7) IG2: 7.7 (11.3) IG3: 8.1 (11.0) CG: 11.2 (11.5) No statistically significant differences between arms, P NR CAIS-P IG1: 13.5 (10.0) IG2: 9.1 (10.5) IG3: 7.4 (10.2) CG: 15.2 (10.7) IG1 vs. CG: adjusted p=0.27 IG2 vs. CG: b=-6.1, t=-4.0, adjusted P<0.001 IG3 vs. CG: b=-7.7, t=-5.2, adjusted P<0.001 Sleep-related problems, 12 weeks, ITT (IG1=139; IG2=133; IG3=140; CG=76), mean (SD) NR by arm, active treatments (IG1, IG2, IG3) resulted in significantly greater reductions in sleep problems than placebo related to separation, as reported by parents (F=6.52, p=0.01, η²=0.01) but not by children. No significant treatment type x time interactions for parent- or childrated dysregulated sleep. Effect sizes were small to medium and	NR
		differed somewhat by treatment type and informant.	

Abbreviations: CAIS-C=Child Anxiety Impact Scale; CAIS-P=Child Anxiety Impact Scale-Parent; CALIS=Child Anxiety Life Interference Scale; CALIS-C=Child Anxiety Life Interference Scale-Child; CALIS-F=Child Anxiety Life Interference Scale-Parent; CALIS-M=Child Anxiety Life Interference Scale; CALIS-C=Cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; ES=effect size; IG=intervention group; ITT=intent to treat; KQ=key question; LSAS-CA=Liebowitz Social Anxiety Scale for Children and Adolescents; MFQ-C=Mood and Feelings Questionnaire for Children; mITT=modified intent to treat; NA=not available; NR=not reported; NS=not significant; OR=odds ratio; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; QOL=quality of life; QOLI-C= Quality of Life Inventory for Children; SD=standard deviation; SE=standard error; TAU=treatment as usual; WHO-5=World Health Organization Five Item Well-being Index.

Appendix I Table 23. Anxiety Treatment Studies: Suicide-Related Harms and Suicide-Related Withdrawal (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide Related Symptoms
Perrin et al, 2019 ¹²² ISRCTN50951795	IG1: Individual child + parent in-person +internet CBT (N=20) CG: Wait-list control (N=20)	NR One participant withdrew because of the onset of suicidal thoughts in response to a family crisis that began after treatment commenced. The crisis was unrelated to the participant's GAD or treatment.
Strawn et al, 2015 ¹⁴² NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	Suicidal ideation, 10 weeks (event occurred at 3 weeks), ITT (IG=135; CG=137), N (%) IG: 1 (1) CG: 0 NA
Strawn et al, 2020 ¹⁴³ NCT02818751	IG1: Escitalopram (N=26) CG: Placebo (N=25)	Aborted suicide attempt, posttreatment (8 weeks), ITT (IG=26; CG=25), N (%) IG: 1 (3.8) CG: 0 (0)
		Self-injurious behavior, posttreatment (8 weeks), ITT (IG=26; CG=25), N (%) IG: 2 (7.7) CG: 1 (4.0)
		Worsening of suicidality, posttreatment (8 weeks), ITT (IG=26; CG=25), N (%) IG: 6 (23.1) CG: 2 (8.0)
		Emergence or worsening of suicidality did not significantly differ between IG and CG (p=0.449) NR
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30) CG: Wait-list control (N=30)	Risk of suicide, 17 weeks, completers (IG1=27; CG=17), N (%) IG: 0 (0) CG: 2 (4.54) withdrew due to risk of suicide
Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸	IG1: Individual child-focused in-person CBT (N=139) IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	Self-harm behavior without suicidal attempt, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 1 (0.7) IG2: 1 (0.8) IG3: 2 (1.4) CG: 0
Rynn et al, 2015 ²⁰⁹ Gordon-Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078		Suicidal ideation across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 5 (3.6) IG2: 0 IG3: 5 (3.6) CG: 1 (1.3)
		Suicidal attempts, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 0 IG3: 0 CG: 0 AD-generalized anxiety disorder: IG-intervention group: ITT-intent to treat: KO-key question: NR-not reported

Abbreviations: CBT=cognitive behavioral therapy; CG=control group; GAD=generalized anxiety disorder; IG=intervention group; ITT=intent to treat; KQ=key question; NR=not reported.

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal due to AE	Other Harms
Birmaher et al, 2003 ⁷³	IG1: Fluoxetine (N=37) CG: Placebo (N=37)	Time x Treatment for total side effects between groups p=NS Gastrointestinal events, 2 weeks (IG1=35; CG=32), N (%) IG1: 16 (46) CG: 7 (22) p=0.04 Gastrointestinal events, 12 weeks (IG1=35; CG=32), % IG1: 44 CG: 22 p=0.04 Neurological complaints (headaches, drowsiness), 2 weeks (IG1=36; CG=36), N (%) IG1: 16 (44) CG: 5 (14) p=0.04 Excitement, giddiness, or disinhibition, posttreatment (12 weeks) (IG1=36, CG=36), N IG1: 7 CG: 4 p=NS	NR	Patient-initiated withdrawal (behavioral disinhibition and non-specified adverse event), 12 weeks (IG1=37; CG=37), N (calculated %) IG1=6 (16) CG=0 p=NR NR	NR
Black et al, 1994 ⁷⁴	IG1: Fluoxetine (N=6) CG: Placebo (N=9)	NR	NR	Dosage reductions due to perceived side effects, 12 weeks (end of treatment), ITT (IG1=6; CG=9), N (%) IG1: 0 (0) CG: 2 (22.2) NR	Global side effect severity, 12 weeks (end of treatment), ITT (IG1=6; CG=9), mean (SD) IG1: 1.40 (0.55) CG: 1.00 (0.0) p=NS No subgroups of interest reported

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal due to AE	Other Harms
Perrin et al, 2019 ¹²² ISRCTN50951795	IG1: Individual child + parent in-person + internet CBT (N=20) CG: Wait-list control (N=20)	NR	NR	One participant withdrew because of the onset of suicidal thoughts in response to a family crisis that began after treatment commenced. The crisis was unrelated to the participant's GAD or treatment. Withdrawal due to AE, 8 weeks, ITT (IG1=20; CG=20), N (%) IG1: 1 (5) CG: 0 (0)	NR
Pine et al, 2001 ¹²⁴ Walkup et al, 2001 ²¹³ Ginsburg et al, 2006 ²¹⁴ Reinblatt et al, 2009 ²¹⁵	IG1: Fluvoxamine (N=63) CG: Placebo (N=65)	NR	NR	Withdrawal due to AE, 8 weeks, ITT (IG1=63; CG=65), N (%) IG1: 5 (8) CG: 1 (2)	Abdominal discomfort IG1: 31 (49) CG: 18 (28) p=0.02 The following other harms were reported but findings were not significant between groups: headache, increased motor activity, insomnia, nasal congestion, drowsiness, nausea, diarrhea, influenza, or URI No subgroups of interest reported

Author, Year,	Treatment Interventions and				
Registry Number	Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal due to AE	Other Harms
Rynn et al, 2001 ¹³⁰	IG1: Sertraline (N=11)	Total AEs NR: Fisher's exact tests	NR	NR	NR
	CG: Placebo (N=11)	(p<0.05) showed no statistically			
		significant differences in adverse			
		events between the sertraline			
		group and the placebo group			
		Dizziness, 9 weeks, ITT (IG=11;			
		CG=11), N (%) IG: 2 (18)			
		CG: 7 (64.4)			
		P<0.08			
		Nausea, 9 weeks, ITT (IG=11;			
		CG=11), N (%)			
		IG: NR (5)			
		CG: 6 (55)			
		P<0.06			
		Stomach pain, 9 weeks, ITT			
		(IG=11; CG=11), N (%)			
		ÌG: 2 (18)			
		CG: 7 (64)			
		P<0.08			
		Dry mouth, 9 weeks, ITT (IG=11;			
		CG=11), N (%)			
		IG: 6 (55)			
		CG: 3 (27)			
		p=0.39			
		Drowsiness, 9 weeks, ITT (IG=11;			
		CG=11), N (%)			
		IG: 8 (73)			
		CG: 5 (45)			
		p=0.39			
		Leg spasms, 9 weeks, ITT (IG=11; CG=11), N (%)			
		IG: 4 (36)			
		CG: 1 (9)			
		p=0.31			
		Restlessness, 9 weeks, ITT			
		(IG=11; CG=11), N (%)			
		IG: 6 (55)			
		CG: 3 (27)			
		p=0.39 ´			

Author, Year,	Treatment Interventions and	ions and			
Registry Number	Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal due to AE	Other Harms
Salzer et al, 2018 ⁴² . ISRCTN 22752528	IG1: Individual child- focused in-person CBT (N=34) CG: Wait-list control (N=39)	Any AE, posttreatment, ITT (IG1=34; CG=39), N (%) IG1: 1 (3) CG: 3 (8) P=NS	Any SAE, posttreatment, ITT (IG1=34; CG=39), N (%) IG1: 0 CG: 1 (3) Note: the article calls this an SAE, it was hospitalization due to the need to remove a dental brace	NR	NR
Stjerneklar et al, 2019 ¹⁴¹ NCT02535403	IG1: Individual child- focused internet CBT (N=35) CG: Wait-list control group (N=35)	Any AE, 14 weeks—study only reports that 1 participant in CG dropped out due to worsening of symptoms	NR	Patient-initiated dropout, 14 weeks, 1 participant in CG due to worsening in symptoms and offered treatment through the municipality NR	NR
Strawn et al, 2015 ¹⁴² NCT01226511	IG1: Duloxetine (N=135) CG: Placebo (N=137)	Treatment-emergent AEs, 10 weeks, ITT (IG=135; CG=137), N (%) IG: 106 (78.5) CG: 90 (65.7) p=0.22	Serious adverse event, 10 weeks, ITT (IG=135; CG=137), N (%) IG: 1 (0.7) CG: 0 (0)	Discontinuation because of an AE, 10 weeks, ITT (IG=135; CG=137), N (%) IG: 7 (5.2) CG: 6 (4.4) p=0.784 NA	Mortality, 10 weeks, ITT (IG=135; CG=137), N (%) IG: 0 CG: 0
Strawn et al, 2020 ¹⁴³ NCT02818751	IG1: Escitalopram (N=26) CG: Placebo (N=25)	NR for overall, only reported by system organ class; "did not differ between groups with the exception of bruising."	Serious adverse event, 8 weeks, ITT (IG=26; CG=23), N (%) IG: 1 (3.8) CG: 1 (4.0)	Discontinued due to serious adverse event, posttreatment (8 weeks), ITT (IG=26; CG=25), N (%) IG: 1 (3.8) CG: 1 (4.0) NR	C-SSRS-defined worsening, posttreatment (8 weeks), ITT (IG=26; CG=25), N (%) IG: 6 (23.1) CG: 2 (8.0) No subgroups of interest reported
Waite et al, 2019 ¹⁵² ISRCTN79652741	IG1: Individual child + parent internet CBT (N=30) CG: Wait-list control (N=30)	NR	NR	Risk of suicide, 17 weeks, completers (IG1=27; CG=17), N (%) IG: 0 (0) CG: 2 (4.54) withdrew due to risk of suicide	NR

	Treatment				
Author, Year,	Interventions and	Incidence Any AEs	Incidence of SAEs	Withdrawal due to AE	Other Harms
Registry Number Walkup et al, 2008 ¹⁵³ Albano et al, 2018 ²⁰⁵ Taylor et al 2018 ²⁰⁶ Compton et al, 2014 ²⁰⁷ Caporino et al, 2017 ²¹⁶ Sachez et al, 2019 ²⁰⁸ Rynn et al, 2015 ²⁰⁹ Gordon- Hollingsworth et al, 2015 ²¹⁰ Ginsburg et al, 2011 ²¹¹ NCT00052078	Comparators IG1: Individual child- focused in-person CBT (N=139) IG2: Sertraline (N=133) IG3: CBT + sertraline (N=140) CG: Placebo (N=76)	Incidence Any AEs Any physical AE, across 12 weeks, (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 51 (36.7) IG2: 67 (50.4) IG3: 58 (41.4) CG: 35 (46.1) Any psychiatric adverse events, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 13 (9.4) IG2: 23 (17.3) IG3: 41 (29.3) CG: 10 (13.2) Harm-related adverse events (i.e., self-injurious behavior, homicidal ideation)* across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 8 (5.8) IG2: 3 (2.3) IG3: 14 (10.0) CG: 1 (1.3)	Incidence of SAEs Serious adverse events Psychiatric hospitalization, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 1 (0.8) IG3: 1 (0.7) CG: 0 Medical hospitalization, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 1 (0) IG3: 0 CG: 0	Withdrawal due to AE Withdrawal from treatment due to worsening symptoms, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 0 IG3: 1 (0.7) CG: 1 (1.3) Withdrawal from study due to worsening symptoms, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 1 (0.8) IG3: 1 (0.7) CG: 0	Other Harms Homicidal ideation, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 2 (1.5) IG3: 0 CG: 0 Homicidal attempts, across 12 weeks (IG1=139; IG2=133; IG3=140; CG=76), N (%) IG1: 0 IG2: 0 IG3: 0 CG: 0

^{*} There were no instances of suicidal behavior.

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CG=control group; C-SSRS=Columbia Suicide Severity Rating Scale (C-SSRS; GAD=generalized anxiety disorder; IG=intervention group; ITT=intent to treat; KQ=key question; NA=not applicable; NR=not reported; NS=not significant; SAE=serious adverse event; SD=standard deviation; URI=upper respiratory illness.

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Clarke et al, 2016 ⁷⁵ NCT00523081	U.S. RCT Kaiser Permanente Center for Health Research	Reviewed HMO Electronic Medical Record then sought primary care provider permission	IG1: CBT + TAU (N=106) Description: Two, 4-session modules: CT (cognitive therapy) and BA (behavioral activation). Intervention terminates after first module if nearly or completely recovered Duration: 4 to 8 sessions of CBT (duration not specified)	CG: TAU (N=106) Participants permitted to continue and or initiate any nonresearch mental health or general medical treatment	Some concerns
Clarke et al, 2005 ⁷⁶ R01-HS10535, HS13854	U.S. RCT AHRQ and Garfield Memorial Fund	Pediatric clinics in a health maintenance organization	IG1: Brief CBT + TAU SSRI (N=77) Description: Between five and nine 60-minute sessions of individual CBT in initial phase, if recovered, did not receive the 2nd module. If not recovered, progressed to remaining module of sessions 6 to 9. Also acute phase aimed to maximize SSRI benefits through targeting medication adherence and consultation with PCP about dosing. Monthly informational parent meetings. There was a continuation phase CBT with brief check-in phone calls at 1, 2, 3, 5, 7, and 9 months following acute phase	CG: TAU + SSRI (N=75) Treatment as Usual SSRIs - permitted to receive any nonstudy healthcare services or medications including the index SSRI medication	Some concerns
Clarke et al, 1999 45	U.S. RCT NIMH	Recruited at 2 sites via announcements to health professionals and school counselors, television and newspaper stories, and advertisements	IG1: Group CBT (N=45) Description: Group CBT (Adolescent Coping With Depression Course) for adolescents only; no family involvement; mixed-gender groups of 10 adolescents; 16 sessions, each session 2 hours, delivered over 8 weeks; delivered by advanced graduate psychology or social work students or masters- or doctoral-level clinicians, plus 40 hours of specialized training and weekly supervision meetings IG2: Group CBT Plus Parent Sessions (N=42) Description: Group CBT same as IG1 plus 8 weekly 2-hour parent sessions (6 separate, 2 held jointly with adolescent group) over 8 weeks	CG: Wait-list (N=36) At the end of the 8 weeks, participants were offered nonexperimental treatment	Some concerns

Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
U.S. RCT Forest Laboratories	NR	IG1: Escitalopram (N=158) Description: Escitalopram dose was fixed at 10 mg/day for the first 3 weeks of double-blind treatment; dose could be increased to 20 mg/day at the end of week 3 or 4. Dosage could be returned to 10 mg/day if limited by adverse events.	CG: Placebo (N=158) Placebo	Some concerns
U.S. RCT NIMH and National Center for Research Resources	Recruited from community advertisements and clinical referrals	IG1: Family CBT (N=19) Description: Family-based therapy incorporating psychoeducation and CBT techniques into weekly 45- to 50-minute parent and child individual sessions. Parents join for the beginning and end of each child session. Sessions with siblings or school professionals provided as relevant.	CG: Placebo (N=18) Two placebo pills twice daily and a multivitamin/mineral tablet.	Low/some concerns
U.S. RCT NIMH	Recruited from preschools, daycares, primary care, and mental health facilities	IG1: PCIT-ED (N=114) Description: Parent Child Interaction Therapy-Emotion Development (PCIT-ED) is a dyadic parent-child psychotherapy that includes an Emotion Development module after the standard 12 PCIT sessions. Both the standard PCIT and the add-on ED module use the technique of teaching of the parent followed by coaching the parent in interactions with the child in vivo using a bug-in-the-ear device. Therapy is manualized with therapist training and fidelity monitoring procedures. Duration: 20 sessions over 18 weeks	CG: Wait-list (N=115) Wait-list control	Some concerns
	U.S. RCT Forest Laboratories U.S. RCT NIMH and National Center for Research Resources U.S. RCT	Study Design Funding U.S. RCT Forest Laboratories NR Recruited from community advertisements and clinical referrals U.S. Resources Recruited from community advertisements and clinical referrals	U.S. RCT Forest Laboratories U.S. RCT	Study Design Funding Setting Intervention(s) Comparator

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	U.S. RCT NIMH, study drug and placebo provided by Lilly Inc.	Recruited from clinics; newspaper, TV, and radio advertisements; primary care physicians; other mental health clinicians; and schools and juvenile justice facilities at 13 academic and community clinics	IG1: Fluoxetine + CBT (N=107) Description: Combination of fluoxetine and CBT as described in the other study arms. IG2: Fluoxetine + CBT (N=107) Description: Combination of fluoxetine and CBT as described in the other study arms. IG3: Fluoxetine (N=109) Description: Flexible dose of 10 to 40 mg/d based on pharmacotherapist-assigned CGI-S score and assessment of clinically significant AEs. Medication management took place during 6 medication visits lasting 20 to 30 minutes each, and pharmacotherapist offered general encouragement about effectiveness of pharmacotherapy for MDD. Duration: 12 weeks	CG: Placebo (N=112) Placebo for fluoxetine	Some concerns
Mufson et al, 2004 ¹¹⁸ McGlinchey et al, 2017 ²²⁸	U.S. RCT SAMHSA	Five school-based mental health clinics in New York City, NY	IG1: Interpersonal psychotherapy (N=34) Description: Interpersonal psychotherapy modified for depressed adolescents (IPT-A) was manualized treatment to reduce depressive symptoms and improve interpersonal functioning administered during 12 sessions in a 12- to 16-week period. Therapists provided 8 consecutive 35-minute weekly sessions followed by 4 sessions scheduled at any frequency during the ensuing 8 weeks. Duration: 16 weeks	CG: TAU (N=29) The psychological treatment the adolescents would have received in the school-based clinic if the study had not been in place, varied but closely resembled supportive counseling. Most adolescents in the TAU group received individual psychotherapy, 8 received 1 to 3 additional family/parent sessions, and 5 participated in group therapy.	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Richardson et al, 2014 ¹²⁷ NCT01140464	U.S. RCT NIMH	Recruited from 9 pediatric and family care clinics in 3 urban areas in Washington State	IG1: Collaborative care (N=50) Description: ROAD, adapted collaborative care intervention based on the IMPACT Team Care model. Included developmentally sensitive materials and structured involvement of adolescent and parent in the initial education and engagement session, the choice of treatment (antidepressant, brief CBT, or both), and followup contacts. Delivered by master's-level clinicians. Adolescents with a less than 50% decrease in PHQ-9 at 4 to 8 weeksld increase medication dose, add CBT to medication, add medication to CBT, or switch treatments. Those who needed specialty mental health care could be referred at any time. Duration: 12 months	CG: Enhanced Usual Care (N=51) Adolescents and parents received a letter summarizing test results and encouraging followup to initiate depression care. Primary care clinicians received letters summarizing the results and recommending treatment. Group health coverage includes primary care, mental health care, and medications. All patients could self-refer to mental health care through a centralized behavioral health intake line.	Low
Topooco et al, 2018 ¹⁴⁷ NCT02363205	Other very high HDI Sweden RCT Queen Silvia's Jubilee Fund, Swedish Central Bank	Recruited from the community through social media, schools, and organizations for youth mental health	IG1: Internet CBT (N=33) Description: Internet-based CBT consisting of 8 skill-based modules including reading assignments and videos plus 8 weekly 30-minute chat sessions with therapist highly structured to correspond to modules. Techniques included psychoeducation, behavioral activation, cognitive restructuring, affect regulation, anxiety management, and relapse prevention. Duration: 8 weeks	CG: Attention control (N=37) Therapist monitoring and nonspecific counseling to control for time and nonspecific treatment factors. Participants had access to the treatment platform to view depression scores and message their therapist. Participants were instructed to contact their therapist due to deterioration and received nonspecific support. Therapists were instructed not to use specific CBT techniques.	Some concerns

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Topooco et al, 2019 ¹⁴⁸ NCT02363205	Other very high HDI Sweden RCT The Swedish Central Bank	Recruited from the community through social media, schools, youth centers, and clinics across Sweden	IG1: Internet CBT (N=35) Description: Internet-based CBT consisting of 8 skill-based modules including reading assignments and videos plus 8 weekly 45-minute chat sessions with therapist highly structured to correspond to modules. Techniques included psychoeducation, behavioral activation, cognitive restructuring, affect regulation, anxiety management, and relapse prevention. Therapist chat sessions each week conducted within the platform. Duration: 8 weeks	CG: Attention control (N=35) Assigned a therapist, received an introductory personal platform in-mail from therapist, weekly assessments viewed by therapist, informed that therapist might contact them to follow-up on their wellbeing. Participants were allowed to seek regular care, which in Sweden is for free for adolescents.	Some Concerns
Wagner et al, 2006 ¹⁵¹	U.S. RCT Forest Laboratories	25 sites in the U.S.	IG1: Escitalopram (N=132) Description: Escitalopram, flexible dose, 10 to 20 mg/day based on clinical response and tolerability. Duration: 8 weeks	CG: Placebo (N=136) Placebo	Some concerns

Abbreviations: AE=adverse event; AHRQ=Agency for Healthcare Research and Quality; BA=behavioral activation; CBT=cognitive behavioral therapy; CG=control group; CGI-S=Clinical Global Impressions-Severity; CT=cognitive therapy; ED=emergency department; HDI=Human Development Index; HMO=health maintenance organization; IG=intervention group; IMPACT= Improving Mood-Promoting Access to Collaborative Treatment; IPT-A=Intensive Interpersonal Psychotherapy for Depressed Adolescents with Suicidal Risk; KQ=key question; MDD=major depressive disorder; NIMH=National Institute of Mental Health; NR=not reported; PCIT=Parent Child Interaction Therapy; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PCP=primary care provider; PHQ-9=Patient Health Questionnaire-9 question; RCT=randomized, controlled trial; ROAD= Reaching Out to Adolescents in Distress; SAMHSA=Substance Abuse and Mental Health Services Administration; SSRI=selective serotonin reuptake inhibitor; TAU=treatment as usual; U.S.=United States.

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Clarke et al, 2016 ⁷⁵ NCT00523081	Mean age (SD): 14.6 (1.7) N (%) Female: 145 (68.4) Race/Ethnicity: Hispanic: 34 (16) Racial minority status: 25 (11.8)	Ages 12 to 18 years meeting DSM-IV criteria for major depression and recently declined antidepressants or discontinued prematurely (<30 days)	Current antidepressant use, bipolar disorder, any psychotic disorder, mental retardation (IDD), autism spectrum disorder, imminent suicide risk, or received >/=CBT	MDD: 100%
Clarke et al, 2005 ⁷⁶ R01-HS10535, HS13854	Mean age (SD): 15.3 (1.6) N (%) Female: 120 (79) Race/Ethnicity: NR	Ages 12 to 18 years with a confirmed DSM episode of major depression who had been dispensed SSRIs	Chart indication of schizophrenia or significant developmental or intellectual disability	MDD: 100%
Clarke et al, 1999 ⁴⁵ None NA	Mean age (SD): 16.2 (1.3) completers N (%) Female: 87 (71) completers Race/Ethnicity: NR	Ages 14 to 18 years with a current DSM-III-R diagnosis of major depressive disorder or dysthymia	Current mania/hypomania, panic disorder, GAD, conduct disorder, psychoactive substance abuse/dependence, lifetime organic brain syndrome, mental retardation, or schizophrenia; receiving other treatment for depression and unwilling to discontinue; or needed immediate, acute treatment.	Primary diagnosis (% completers) MDD: 76% Dysthymia: 13% Comorbid MDD/Dysthymia: 11% Other comorbid disorders Current anxiety disorder: 24% History of nonaffective psychiatric disorder: 24% Recurrent affective disorder: 47%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Emslie et al, 2009 ⁸⁶ Findling, 2013 ²²⁷ NCT00107120	Mean age (SD): IG1: 14.7 (1.6) CG: 14.5 (1.5) N (%) Female: IG1: 92 (59) CG: 92 (59) Race/Ethnicity: White IG1: 113 (73) CG: 123 (78)	Ages 12 to 17 years meeting diagnostic criteria for MDD (DSM-IV) with duration of current episode at least 12 weeks based on K-SADS-PL; score ≥45 on the CDRS-R at screening and baseline; CGI-S score ≥4, Kaufman Brief Intelligence Test score ≥80; normal physical examination, laboratory tests, and ECG at screening. Caregiver capable of providing information about patient's condition. Family support to guarantee adequate safety monitoring.	Principal diagnosis meeting DSM-IV criteria for an Axis I disorder other than MDD; or met DSM-IV criteria at screening for ADD/ADHD, OCD, PTSD, bipolar disorder, pervasive developmental disorder, mental retardation, conduct disorder, or oppositional defiant disorder; history of any psychotic disorder, as defined by DSM-IV or seizures; personality disorder of sufficient severity to interfere with participation, past year history of anorexia nervosa, bulimia, or substance abuse or dependence (including alcohol); first-degree relative with bipolar disorder, considered suicide risk by investigators, positive test for alcohol or other prohibited medication on urine drug screen, not been treated with any antidepressant or anxiolytic medication within 2 weeks of baseline (4 weeks for fluoxetine), any neuroleptic or stimulant within 6 months of screening, or any investigational drug within 30 days or 5 half-lives before screening; been in a previous clinical study of citalopram or escitalopram, history of hypersensitivity reaction to any SSRI; failed to respond to an adequate trial of escitalopram or citalopram or to adequate trials of two other SSRIs; pregnant women or nursing mothers; and female subjects of childbearing potential not practicing a reliable birth control method.	Recurrent MDD: 29% Previous and/or ongoing secondary psychiatric disorders: 15% Antidepressant naive: 83%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Fristad et al, 2019 ⁹⁰ NCT01341925	Mean age (SD): IG1: 11.7 (2.1) CG: 11.1 (2.4) N (%) Female: IG1: 10 (52) CG: 5 (27) Race/Ethnicity: Black IG1: 5 (26) CG: 4 (22) White IG1: 11 (58) CG: 12 (67) Asian IG1: 0 CG: 0 Biracial IG1: 3 (15) CG: 2 (11) Hispanic IG1: 2 (11) CG: 1 (6)	Ages 7 to 14 years diagnosed with MDD, DD, or DDNOS based on the DSM-IV-TR and a CDRS-R score ≥40 and at least 1 caregiver able to participate in followup procedures	Inability to swallow capsules, DSM-IV-TR autistic disorder, psychosis warranting antipsychotic medication, active suicidal concern, active psychotherapy or pharmacotherapy other than stable doses, ADHD or sleep aid medication, IQ <70, or lack of access to a phone	Anxiety disorder IG1: 79% CG: 78% ADHD IG1: 63% CG: 72% Disruptive behavior disorder IG1: 32% CG: 33% PTSD IG1: 16% CG: 11%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Luby et al, 2018 ¹¹¹ NCT02076425	Mean age (SD): IG1: 5.1 (1.0) CG: 5.3 (1.1) N (%) Female: IG1: 38 (33) CG: 42 (36) Race/Ethnicity: African American IG1: 9 (8) CG: 17 (15) Caucasian IG1: 94 (82) CG: 82 (72) Asian IG1: 1 (1) CG: 0 More than 1 race IG1: 10 (9) CG: 16 (14)	Ages 3 to 6 years meeting early-onset MDD symptoms on the Preschool Age Psychiatric Assessment and subsequently diagnosed with MDD using K-SADS-EC by clinician.	Autism spectrum disorder, a serious neurological or chronic medical disorder; significant developmental delay; taking antidepressant medications or in ongoing psychotherapy; on unstable doses of other psychotropic medications; unstable caregiving; or depression judged as too severe to wait for 18 weeks for treatment	Anxiety IG1: 40% CG: 43% ADHD IG1: 46% CG: 33% Mania/hypomania IG1: 2 CG: 2 ODD IG1: 51 CG: 49 Conduct disorder IG1:3 CG: 3
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	Mean age (SD): 14.6 (1.5) N (%) Female: 236 (54.4) Race/Ethnicity: White: 320 (73.8) Black: 57 (12.5) Hispanic: 40 (8.9)	Ages 12 to 17 years meeting DSM-IV criteria for MDD, CDRS-R score of ≥45, IQ of ≥80, and not taking antidepressants. Stable ADHD medications were permitted.	Current or past diagnosis of bipolar disorder, severe conduct disorder, current substance abuse or dependence, PDD, thought disorder, concurrent treatment with psychotropic medication or psychotherapy outside the study, 2 failed SSRI trials, a poor response to clinical treatment containing CBT for depression, intolerance to fluoxetine, confounding medical condition, non-English speaking patient or parent, or pregnancy or refusal to use birth control	Primary/target condition MDD: 100% Other comorbid conditions Anxiety: 27% Disruptive behavior: 24% ADHD: 14% OCD: 3% Substance use: 2%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Mufson et al, 2004 ¹¹⁸ McGlinchey et al, 2017 ²²⁸	Mean age (SD): 15.1 (1.9) N (%) Female: 53 (84) Race/Ethnicity: Hispanic IG1: 26 (76.5) CG: 19 (65.5)	Ages 12 to 18 years, referred to mental health clinics in 1 of 5 school-based health clinics with a HAM-D score ≥10 and a CGAS store ≤64 at screening, DSM-IV diagnosis of MDD, dysthymia, adjustment disorder with depressed mood, or DDNOS.	Actively suicidal or mentally retarded, life threatening medical condition, substance use disorder diagnosis, psychosis, schizophrenia, current treatment for depression, or taking antidepressants.	Primary/target condition % Major depression IG1: 53% CG: 48% Dysthymic disorder IG1: 15% CG: 21% Double depression IG1: 6% CG: 7% DDNOS IG1: 12% CG: 10% Adjustment disorder with depressed mood IG1: 15% CG: 14% Other comorbid conditions % Anxiety disorders: 32% ODD: 16% Substance use: 16% ADHD: 6%
Richardson et al, 2014 ¹²⁷ NCT01140464	Mean age (SD): 15.3 (1.3) N (%) Female: 73 (72) Race/Ethnicity: White: 70 (69) Black: 5 (5) Asian/Pacific Islander: 2 (2) Other/multiracial: 24 (24)	Ages 13 to 17 years meeting MDD criteria on the K-SADS or a PHQ-9 ≥10 on 2 occasions with a CDRS-R score of >42. Adolescents taking antidepressants or receiving psychotherapy who were still symptomatic were eligible to participate.	Non-English speaking, suicidal plan or recent attempt, bipolar, drug/alcohol misuse (CRAFFT score ≥5), seeing a psychiatrist, or developmental delay.	Primary/target condition % Major depression K-SADS scale: 60% Treatment for depression/anxiety in prior 6 months: 39% Antidepressants in 6 months prior to baseline: 25% Undergoing active treatment at start of study: 17% Other comorbid conditions % Brief SCARED score ≥3: 72%

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Topooco et al, 2018 ¹⁴⁷ NCT02363205	Mean age (SD): IG1: 17.2 (1.0) CG: 16.9 (1.1) N (%) Female: IG1: 31 (94) CG: 35 (95) Race/Ethnicity: NR	Ages 15 to 19 years with a score of 14 or more on the BDI-II; at least 5 MDD symptoms or meeting MDD diagnosis on the MINI 6.0 (cut-off ≤16); adolescents with comorbid anxiety disorders included if depression was the primary concern; adolescents on medication for ADHD, anxiety, or depression included if dose was fixed in the past month and constant through study.	Severe suicidal ideation; severe comorbid psychiatric condition that might interfere with the treatment (e.g., bipolar disorder or schizophrenia); currently undergoing psychotherapy treatment; other medical problems that would require other treatments; or currently meeting diagnostic criteria for alcohol or substance misuse	Primary/target diagnosis MDD IG1: 85% CG: 68% Other comorbid conditions Anxiety IG1: 73% CG: 78%
Topooco et al, 2019 ¹⁴⁸ NCT02363205	Mean age (SD): IG1: 17.5 (1.1) CG: 17.5 (1.2) N (%) Female: IG1: 32 (91) CG: 35 (100) Race/Ethnicity: NR	Ages 15 to 19 years with a score of 14 or more on the BDI-II; at least 4 symptoms including 1 core symptom, or fulfilled criteria for MDD according to the MINI clinical interview; adolescents with comorbid anxiety disorders included if depression was the primary concern; adolescents on medication for ADHD, anxiety, or depression included if dose was stable for the previous month.	Adolescents receiving psychological therapy, were alcohol or drug dependent, showed severe suicidal ideation, or who had severe comorbid psychiatric conditions (e.g., bipolar disorder or psychotic symptoms).	Primary/target condition % MDD IG1: 77 CG: 74 Other comorbid conditions % Anxiety IG1: 71 CG: 69

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
Wagner et al, 2006 ¹⁵¹	Mean age (SD): 12.3 (3.0) N (%) Female: 137 (52) Race/Ethnicity: White IG1: 93 (71) CG: 95 (71) Black IG1: 19 (15) CG: 17 (13) Asian IG1: 1 (1) CG: 2 (2) Other IG1: 18 (14) CG: 19 (14)	Ages 6 to 17 years, DSM-IV criteria for MDD, current episode at least 4 weeks duration, normal physical examination, laboratory tests, and EKG	Any primary psychiatric diagnosis other than MDD, any psychotic features, any severe personality disorder, ADHD, PTSD, bipolar disorder, PDD, mental retardation, conduct disorder, oppositional defiant disorder, eating disorder, substance abuse including alcohol within the past year; not practicing birth control, pregnant, or nursing; no psychotherapy or behavioral therapy within previous 3 months; hospitalized because of a suicide attempt or serious suicide attempts within the past year; treated with any antidepressant or anxiolytic medication within 2 weeks of baseline (4 weeks for fluoxetine), treatment with an antipsychotic or stimulant within 6 months before screening, receipt of an investigational drug 30 days before study entry, failure of adequate trial of escitalopram or citalopram or adequate trials of 2 other SSRIs, concomitant treatment with any psychotropic drug other than zolpidem or zaleplon for insomnia	Primary/target condition: MDD: 100%

Abbreviations: ADD=attention deficit disorder; ADHD=attention deficit hyperactivity disorder; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; CGAS=Children's Global Assessment Scale; CGI-S=Clinical Global Impressions-Severity; DD=depressive disorder; DDNOS=depressive disorders not otherwise specified; DSM=Diagnostic and Statistical Manual of Mental Disorders; DSM-III-R=Diagnostic and Statistical Manual of Mental Disorders-4th edition-Revised; DSM-IV-TR=Diagnostic and Statistical Manual of Mental Disorders-4th edition-Revised, Text Revision; ECG=electrocardiogram; EKG=electrocardiogram; GAD=generalized anxiety disorder; HAM-D=Hamilton Depression Rating Scale; IDD=intellectual and developmental disability; IG=intervention group; IQ=intelligence quotient; KQ=key question; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children; K-SADS-EC=Schedule For Affective Disorders And Schizophrenia For School-Age Children-Early Childhood version; K-SADS-PL= Schedule For Affective Disorders And Schizophrenia For School-Age Children-Present and Lifetime version; MDD=major depressive disorder; MINI=Mini International Neuropsychiatric Interview; NA=not available; NR=not reported; OCD=obsessive compulsive disorder; ODD=oppositional defiant disorder; PDD=persistent depressive disorder; PHQ-9=Patient Health Questionnaire-9 question; PTSD=post-traumatic stress disorder; SCARED=Screen for Anxiety Related Emotional Disorders; SD=standard deviation; SSRI=selective serotonin reuptake inhibitor.

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Clarke et al, 2016 ⁷⁵ NCT00523081	IG1: CBT + TAU (N=106) CG: TAU (N=106)	CDRS, posttreatment (52 weeks and 104 weeks), ITT (IG1=106; CG=106), mean (SD) 52 weeks IG1: 30.14 (11.26) CG: 28.24 (10.54) Effect size d=0.278; mean difference: 2.25 (95% CI, -4.45 to 0.05) P<0.04 favoring CBT
		104 weeks IG1: 28.11 (9.88) CG: 29.17 (10.79) Effect size d=0.145; mean difference: -1.30 (95% CI, -3.73 to 1.14) P<0.36
		CES-D, posttreatment (52 weeks and 104 weeks), ITT (IG1=106; CG=106), mean (SD) 52 weeks IG1: 22.59 (7.00) CG: 22.51 (7.43) Effect size d=0.394; mean difference: -2.88 (95% CI: -4.87 to -0.89) P<0.005 favoring CBT
		104 weeks IG1: 21.46 (7.44) CG: 21.91 (6.95) Effect size d=0.055; mean difference: -0.32 (95% CI: -1.91 to 1.27) P=0.62
Clarke et al, 2005 ⁷⁶ R01-HS10535, HS13854	IG1: Brief CBT + TAU SSRI (N=77) CG: TAU + SSRI (N=75)	CES-D scores posttreatment change from baseline to followup at week 52, completers (IG=53; CG=50), mean (SD) IG1: 11.5 (11.0) CG: 14.9 (10.1) Effect size=0.17, F=3.2 Time x Treatment interaction p=0.07 (no differences between CBT+SSRI vs. TAU+SSRI)
		HAM-D scores posttreatment change from baseline to followup at week 52, completers (IG1=53; CG=50), mean (SD) IG1: 4.9 (7.1) CG: 6.5 (6.6) Effect size=0.054, F=1.0 Time x Treatment interaction p=0.32 (no differences between CBT+SSRI vs. TAU+SSRI)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Clarke et al, 1999 ⁴⁵ None NA	IG1: Group CBT (N=45) IG2: Group CBT plus parent sessions (N=42) CG: Wait-list (N=36)	BDI, posttreatment (8 weeks), completers (IG1=37; IG2=32; CG=27), mean (SD) IG1: 10.1 (9.1) IG2: 13.3 (10.9) CG: 16.0 (11.2)
		IG1/IG2 vs. CG P<0.01; effect size=0.61 HAM-D, posttreatment (8 weeks), completers (IG1=37; IG2=32; CG=27), mean (SD) IG1: 4.6 (4.8) IG2: 6.7 (7.1) CG: 7.7 (7.0) IG1/IG2 vs. CG P NS
Emslie et al, 2009 ⁸⁶ Findling, 2013 ²²⁷ NCT00107120	IG1: Escitalopram (N=158) CG: Placebo (N=158)	CDRS-R, change from baseline to 8 weeks, ITT (IG1=154; CG=157), mean difference (SE) IG1: -22.1 (1.22) CG: -18.8 (1.27) LSMD (95% CI): -3.356 (-6.226 to -0.486); P=0.022, ES=0.27 CGI-I, 8 weeks, ITT (IG1=154; CG=157), mean difference (SE)
		IG1: 2.2 (0.11) CG: 2.6 (0.11) LSMD (95% CI): -0.344 (-0.595 to -0.092); P=0.008
		CGI-S, change from baseline to 8 weeks, ITT (IG1=154; CG=157), mean difference (SE) IG1: -1.8 (0.11) CG: -1.4 (0.12) LSMD (95% CI): -0.37 (-0.64 to -0.10); P=0.007
Fristad et al, 2019 ⁹⁰ NCT01341925	IG1: Family CBT (N=19) CG: Placebo (N=18)	CDRS-R, posttreatment (12 weeks), ITT (IG1=18; CG=18), mean (SD) IG1: 30 (9) CG: 31 (11) Between-group change Cohen's d=0.04; P=0.880
Luby et al, 2018 ¹¹¹ NCT02076425	IG1: PCIT-ED (N=114) CG: Wait-list (N=115)	K-SADS-EC MDD core score, change from baseline to post-assessment, ITT (IG1=114; CG=115), adjusted mean difference (SE) 2.34 (0.26) Cohen's d=1.01; P<0.0001
		PFC-scale, change from baseline to post-assessment, ITT (IG1=114; CG=115), adjusted mean difference (SE) 11.91 (1.29) Cohen's d=1.04; P<0.0001
		Controlling for baseline characteristics, gender, and baseline externalizing disorder.

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸	IG1: Fluoxetine + CBT (N=107) IG2: Fluoxetine + CBT (N=107) IG3: Fluoxetine (N=109) CG: Placebo (N=112)	CDRS-R, 6 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), adjusted mean (SD) IG1: 38.10 (7.78) IG2: 39.80 (7.37) IG3: 44.63 (8.30) CG: 44.90 (7.32)
Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286		CDRS-R total, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), adjusted mean (SD) IG1: 33.79 (8.24) IG2: 36.30 (8.18) IG3: 42.06 (9.18) CG: 41.77 (7.99)
		Across 12 weeks time-by-treatment interaction P=0.001 based on linear random coefficient regression; planned pairwise comparisons IG1 vs. CG; P=0.001 IG2 vs. CG; P=0.10 IG3 vs. CG; P=0.40
		Supplemental between-group comparisons of means at 12 weeks IG1 vs. CG; P=0.001 IG2 vs. CG; P=0.002 IG3 vs. CG; P=0.97
		RADS, 6 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), adjusted mean (SD) IG1: 60.90 (11.59) IG2: 63.41 (12.44) IG3: 69.10 (13.59) CG: 69.43 (10.94)
		RADS, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), adjusted mean (SD) IG1: 56.95 (12.24) IG2: 60.58 (13.07) IG3: 67.96 (14.18) CG: 66.68 (11.41)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286 (continued)		Across 12 weeks time-by-treatment interaction P=0.001; based on linear random coefficient regression, planned pairwise comparisons IG1 vs. CG; P=0.001 IG2 vs. CG; P=0.34 IG3 vs. CG; P=0.21 Supplemental between-group comparisons of means at 12 weeks IG1 vs. CG; P=0.001 IG2 vs. CG; P=0.003 IG3 vs. CG; P=0.94 NOTE: Means adjusted for both fixed (treatment and time) and random (participant and site) effects derived from linear random coefficient model
Mufson et al, 2004 ¹¹⁸ McGlinchey et al, 2017 ²²⁸	IG1: Interpersonal psychotherapy (N=34) CG: TAU (N=29)	BDI, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD) IG1: 8.4 (11.0) CG: 12.3 (9.7) P=0.14, effect size=0.37 Repeated measures ANOVA Time x Treatment interaction P=0.04 CGI-I, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD) IG1: 2.3 (1.3) CG: 3.1 (1.6) P=0.03, effect size=0.59 (95% CI, 0.24 to 0.94) CGI-S, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD) IG1: 2.3 (1.3) CG: 3.0 (1.4) P=0.03, effect size=0.48 (95% CI, 0.15 to 0.81) HAM-D, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD) IG1: 8.7 (8.0) CG: 12.8 (8.4) P=0.04, effect size=0.50 Repeated measures ANOVA Time x Treatment interaction P=0.003 HAM-D, week 16, mITT (IG1=33; CG=29), mean (SD) IG1: 6.9 (NR) CG: 10.6 (NR) P=0.04, effect size=0.51 (95% CI, 0.003 to 1.02)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Richardson et al, 2014 ¹²⁷ NCT01140464	IG1: Collaborative care (N=50) CG: Enhanced usual care (N=51)	Modified CDRS-R, 6 months, ITT (IG1=50; CG=51), mean difference between groups (95% CI) -8.5 (-13.4 to -3.6), P=0.001
		Modified CDRS-R, posttreatment (12 months), ITT (IG1=50; CG=51), mean (95% CI) IG1: 27.5 (23.8 to 31.1) CG: 34.6 (30.6 to 38.6)
		Modified CDRS-R, posttreatment (12 months), ITT (IG1=50; CG=51), mean difference between groups (95% CI) -9.4 (-15.0 to -3.8), P=0.001
Topooco et al, 2018 ¹⁴⁷ NCT02363205	IG1: Internet CBT (N=33) CG: Attention control (N=37)	BDI-II, posttreatment (8 weeks), ITT (IG1=33; CG=37), mean (SD) IG1: 19.9 (7.2) CG: 25.2 (7.8) Between-group Cohen's d (95% CI), baseline to 8 weeks: 0.71 (0.22 to 1.19), P<0.05
		PHQ-9, posttreatment (8 weeks), ITT (IG1=33; CG=37), mean (SD) IG1: 9.7 (2.9) CG: 10.8 (3.0) Between-group Cohen's d (95% CI), baseline to 8 weeks: 0.36 (-0.10 to -0.84), P=NS
Topooco et al, 2019 ¹⁴⁸ NCT02363205	IG1: Internet CBT (N=35) CG: Attention control (N=35)	BDI-II, posttreatment (week 8), ITT (IG1=35; CG=35), mean (SD) IG1: 16.0 (11.3) CG: 24.8 (10.4) Between-group change from baseline ES NR; P<0.001
		MFQ, posttreatment (week 8), ITT (IG1=35; CG=35), mean (SD) IG1: 24.3 (12.8) CG: 31.0 (9.8) Between-group change from baseline ES NR; P<0.01

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
Wagner et al, 2006 ¹⁵¹	IG1: Escitalopram (N=132) CG: Placebo (N=136)	CDRS-R, baseline to posttreatment (8 weeks), ITT/LOCF (IG1=129; CG=132), adjusted mean change IG1: -21.9 CG: -20.2 P=0.31
		CGI-S, baseline to posttreatment (8 weeks), ITT/LOCF (IG1=129; CG=132), adjusted mean change IG1: -1.6 CG: -1.3 P=0.057
		CGI-I, posttreatment (8 weeks), ITT/LOCF (IG1=129; CG=132), adjusted mean IG1: 2.3 CG: 2.5 P=0.169

Abbreviations: ANOVA=analysis of variance; BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS=Children's Depression Rating Scale; CDRS-R=Children's Depression Rating Scale-Revised; CES-D=Center for Epidemiological Studies-Depression; CG=control group; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CI=confidence interval; ES=effect size; HAM-D=Hamilton Depression Rating Scale; IG=intervention group; ITT=intent to treat; KQ=key question; K-SADS-EC=Schedule For Affective Disorders And Schizophrenia For School-Age Children-Early Childhood version; LOCF=last observation carried forward; LSMD=least-square mean difference; MDD=major depressive disorder; MFQ=Mood & Feelings Questionnaire; mITT=modified intent to treat; NA=not available; NR=not reported; NS=not significant; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PFC=Preschool Feelings Checklist; PHQ-9=Patient Health Questionnaire-9 question; RADS=Reynolds Adolescent Depression Scale; SD=standard deviation; SE=standard error; SSRI=selective serotonin reuptake inhibitor; TAU=treatment as usual.

Appendix I Table 28. Depression Treatment Studies: Anxiety-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
Topooco et al, 2018 ¹⁴⁷ NCT02363205	IG1: Internet CBT (N=33) CG: Attention control (N=37)	BAI, posttreatment (8 weeks), ITT (IG1=33; CG=37), mean (SD) IG1: 20.6 (9.0) CG: 19.4 (8.6) Between-group Cohen's d (95% CI), baseline to 8 weeks: 0.14 (-0.33 to -0.60)
		SIAS, posttreatment (8 weeks), ITT (IG1=33; CG=37), mean (SD) IG1: 39.3 (1)
Topooco et al, 2019 ¹⁴⁸ NCT02363205	IG1: Internet CBT (N=35) CG: Attention control (N=35)	BAI, posttreatment (week 8), ITT (IG1=35; CG=35), mean (SD) IG1: 16.6 (10.3) CG: 20.0 (9.3) Between-group change from baseline ES NR; P NS
		SIAS, week 8, ITT (IG1=35; CG=35), mean (SD) IG1: 35.4 (19.0) CG: 35.1 (14.3) Between-group change from baseline ES NR; P NS

Abbreviations: BAI=Beck Anxiety Inventory; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; ES=effect size; IG=intervention group; ITT=intent to treat; KQ=key question; NR=not reported; NS=not significant; SD=standard deviation; SIAS=Social Interaction Anxiety Scale.

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Clarke et al, 2016 ⁷⁵ NCT00523081	IG1: CBT + TAU (N=106) CG: TAU (N=106)	Response Major depression diagnostic response defined as ≥8 weeks below the threshold of 5 or more major depressive symptoms necessary for full diagnosis, but where full recovery has not yet occurred Time to response
		MDD response, 52 weeks, ITT (IG1=106; CG=106), mean (SD) 52 weeks IG1: 90 (90.9) CG: 87 (87.9) NNT: 34, OR: 1.39 (95% CI, 1.03 to 1.87)
		MDD response, 104 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 93 (93.9) CG: 91 (91.9) NNT: 50, OR: 1.38 (95% CI, 1.03 to 1.84) NNT ranged from 5 at posttreatment to 50 at the final followup point (week 102)
		Time to response IG1: Average of 13.3 weeks until response (95% CI, 10.6 to 15.9 [median, 9 weeks]) CG: Average of 18 weeks until response (95% CI, 14.7 to 21.3 [median, 12 weeks])
		Remission Recovery defined as ≥8 weeks of no or minimal symptoms (K-SADS Diagnostic Status Rating ≤1-2) and little or no impairment Time to recovery MDD recovery, 104 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 79 (79.8) CG: 68 (68.7) NNT: 10, OR: 1.60 (95% CI, 1.15 to 2.21)
		MDD recovery, 104 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 88 (88.9) CG: 78 (78.8) NNT: 10, OR: 1.59 (95% CI, 1.17 to 2.17)
		Time to recovery IG1: Average of 22.6 weeks to recovery (95% CI ,18.8 to 26.5 [median, 15 weeks]) CG: Average of 30 weeks to recovery (95% CI, 25.3 to 34.7 [median, 23 weeks])

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

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Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Clarke et al, 2005 ⁷⁶ R01-HS10535, HS13854	IG1: Brief CBT + TAU SSRI (N=77) CG: TAU + SSRI (N=75)	Response Number of cases that moved over time from the disordered to the nondisordered CES-D ranges, using "moderately depressed" cutoff score of ≥16 and a "seriously depressed" score ≥24 Loss of depression (from moderately depressed to nondisordered range) CES-D ≥16 at 52 weeks, completers (IG1=53; CG=50), N (%) IG1: 13 (25) CG: 22 (44) Chi square=4.3, p=0.04 favoring CBT No differences at higher cut off level of ≥24 (scores not reported) Remission Number of cases that moved over time from the disordered to the nondisordered CES-D ranges Same as above Other outcomes
		Recurrence: Recurrence within 52 weeks among those who had recovered from their depression episode Recurrence of depression among those who had recovered 32 (24%) of 135, N by group NR IG1: 16 (not calculable) CG: 16 (not calculable) Chi squared=0.01, p=0.76
Clarke et al, 1999 ⁴⁵ None NA	IG1: Group CBT (N=45) IG2: Group CBT plus parent sessions (N=42) CG: Wait-list (N=36)	Loss of diagnosis No longer meeting DSM-III-R criteria for MDD or dysthymia Absence of MDD/dysthymia diagnoses, posttreatment (8 weeks), completers (IG1=37; IG2=32; CG=27), N (%) IG1: 24 (64.9) IG2: 22 (68.8) Combined IG1/IG2: 46 (66.7) CG: 13 (48.1) IG1/IG2 vs. CG, 1 tailed P<0.05; Cohen's h=0.38 OR: 2.15 (90% CI, 1.01 to 4.59)

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Emslie et al, 2009 ⁸⁶ Findling et al, 2013 ²²⁷ NCT00107120	IG1: Escitalopram (N=158) CG: Placebo (N=158)	Response CGI-I ≤2 CDRS-R (40% decrease) CGI-I ≤2, 8 weeks, ITT (IG1=154; CG=157), N (%) IG1: 99 (64.3) CG: 83 (52.9) P=0.03 CDRS-R (40% decrease), 8 weeks, ITT (IG1=154; CG=157), N (%) IG1: 91 (59.1) CG: 76 (48.4) P=0.06 Remission Defined as CDRS-R ≤28 CDRS-R ≤28, 8 weeks, ITT (IG1=154; CG=157), N (%) IG1: 64 (41.6) CG: 56 (35.7) P=0.15
Fristad et al, 2019 ⁹⁰ NCT01341925	IG1: Family CBT (N=19) CG: Placebo (N=18)	Remission Defined as CDRS-R score ≤28 CDRS-R score ≤28, 12 weeks, ITT (IG1=18; CG=18), N (%) IG1: 11 (61) CG: 10 (56)
Luby et al, 2018 ¹¹¹ NCT02076425	IG1: PCIT-ED (N=114) CG: Wait-list (N=115)	Loss of diagnosis MDD diagnosis K-SADS-EC MDD diagnosis, change from baseline to post assessment (18 weeks), ITT (IG1=114; CG=115), aOR (95% CI) CG vs. IG1: 9.52 (8.44 to 10.74); P<0.0001 K-SADS-EC MDD diagnosis, change from baseline to post assessment, completers (IG1=100; CG=91), N (%), aOR (95% CI) IG1: 68 (75) CG: 22 (22) CG vs. IG1: 12.15 (5.95 to 24.82); P<0.0001 Both analyses controlling for baseline characteristics, gender, and baseline externalizing disorder. K-SADS-EC MDD diagnosis for all participants, multiply imputed.

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Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	IG1: Fluoxetine + CBT (N=107) IG2: Fluoxetine + CBT (N=107) IG3: Fluoxetine (N=109) CG: Placebo (N=112)	Response CGI improvement score of 1 (very much improved) or 2 (much improved) CGI-l positive response, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), % with response (95% CI) adjusted for clinical site IG1: 71.0 (62 to 80) IG2: 60.6 (51 to 70) IG3: 43.2 (34 to 52) CG: 34.8 (26 to 44) P<0.001 Planned pairwise comparisons IG1 vs. CG; P=0.001 IG3 vs. CG; P=0.001 IG3 vs. CG; P=0.001 IG3 vs. CG; P=0.20 Remission CDRS-R score ≤28 CDRS-R score ≤28 CDRS-R score ≤28, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), % IG1: 40 (37) IG2: 25 (23) IG3: 14 (16) CG: 19 (17) CR (95% CI) IG1 vs. CG: 3.0 (1.58 to 5.79); P=0.0009 IG2 vs. CG: 1.5 (0.74 to 2.88); P=0.28 IG3 vs. CG: 0.9 (0.44 to 1.88); P=0.80 Loss of diagnosis Loss of MDD diagnosis based on K-SADS-P/L Loss of MDD diagnosis, 12 weeks (posttreatment), completers (n=379), % IG1: 85.3 IG2: 78.6 IG3: 61.1 CG: 60.4 Overall treatment effect: P<0.0001 OR (95% CI) IG1 vs. CG: 4.1 (2.00 to 8.44); P=0.0001 IG2 vs. CG: 2.4 (1.27 to 4.67); P=0.007 IG3 vs. CG: 2.4 (1.27 to 4.67); P=0.007

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Mufson et al, 2004 ¹¹⁸ McGlinchey et al, 2017 ²²⁸	IG1: Interpersonal psychotherapy (N=34) CG: TAU (N=29)	Remission HAM-D ≤6, posttreatment (week 12), ITT (IG1=34; CG=29), N (%) IG1: 17 (50) CG: 10 (34) P=NR BDI ≤9, posttreatment (week 12), ITT (IG1=34; CG=29), N (%)
		IG1: 25 (74) CG: 15 (52) P=0.048
Richardson et al, 2014 ¹²⁷ NCT01140464	IG1: Collaborative care (N=50) CG: Enhanced usual care (N=51)	Response ≥50% reduction in CDRS-R ≥50% reduction in CDRS-R, 6 months, ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 48.4 CG: 23.4 OR (95% CI): 3.1 (1.2 to 7.9), P=0.02 ≥50% reduction in CDRS-R, posttreatment (12 months), ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 67.6 CG: 38.6 OR (95% CI): 3.3 (1.4 to 8.2), P=0.009 Remission PHQ-9 <5 PHQ-9 <5, 6 months, ITT (IG1=50, CG=51), imputed % based on 20 multiple imputations IG1: 36.6 CG: 10.2 OR: 5.2 (1.6 to 17.3), P=0.007 PHQ-9 <5, posttreatment (12 months), ITT (IG1=50, CG=51), imputed % based on 20 multiple imputations IG1: 50.4

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Richardson et al, 2014 ¹²⁷ NCT01140464 (continued)		Other outcomes Satisfaction with care (moderately to very satisfied) Satisfaction with care (moderately to very satisfied), 6 months, ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 85.8 CG: 52.2 OR (95% CI): 5.6 (1.9 to 16.0), P=0.001 Satisfaction with care (moderately to very satisfied), posttreatment (12 months), ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 82.2 CG: 68.5 OR (95% CI): 2.1 (0.7 to 6.1), P=0.001
Topooco et al, 2018 ¹⁴⁷ NCT02363205	IG1: Internet CBT (N=33) CG: Attention control (N=37)	Response A 30% or more decrease in symptoms on the BDI-II BDI-II ≥30% decrease, posttreatment (8 weeks), ITT (IG1=33; CG=37), N (%) IG1: 20 (60.6) CG: 12 (32.4) P<0.05 Remission 50% or more decrease in symptoms on the BDI-II BDI-II ≥50% decrease, posttreatment (8 weeks), ITT (IG1=33; CG=37), N (%) IG1: 14 (42.4) CG: 5 (13.5) P<0.01
		Loss of diagnosis Loss of MDD diagnosis based on DSM-IV criteria Loss of diagnosis DSM-IV criteria for MDD, posttreatment (8 weeks), ITT (IG1=33; CG=37), N (%) IG1: 20 (71.4) CG: 4 (16.0) P<0.001 Other outcomes Deterioration of 30% or more in BDI-II score
		Deterioration of 30% or more in BDI-II score, completers (IG1=30; CG=36), N (%) IG1: 1 (3) CG: 3 (8) Deterioration of 30% or more in BDI-II score, ITT (IG1=33; CG=37), N (%) IG1: 4 (12) CG: NR

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Topooco et al, 2019 ¹⁴⁸ NCT02363205	IG1: Internet CBT (N=35) CG: Attention control (N=35)	Response Various definitions based on BDI-II criteria BDI-II ≥30% decrease, posttreatment (8 weeks), ITT (IG1=35; CG=35), N (%) IG1: NR CG: NR P=0.004 BDI-II ≥13, posttreatment (8 weeks), ITT (IG1=35; CG=35), N (%) IG1: NR CG: NR P=0.004 BDI-II ≥10, posttreatment (8 weeks), ITT (IG1=35; CG=35), N (%) IG1: NR CG: NR P=0.004 BDI-II ≥10, posttreatment (8 weeks), ITT (IG1=35; CG=35), N (%) IG1: NR CG: NR P≤0.001 Remission Clinically significant improvement defined as scoring 2 SD below the pretreatment mean for both conditions on the BDI-II, while also fulfilling the reliable change index criteria Clinically significant improvement, posttreatment (8 weeks), ITT (IG1=35, CG=35), N (%) IG1: 16 (46) CG: 4 (11) P=0.001 Loss of diagnosis No longer met DSM-5 criteria for MDD among those who met DSM-5 criteria at baseline No longer met MDD criteria, posttreatment (8 weeks), ITT (IG1=27; CG=26), N (%) IG1: 15 (56)
		CG: 7 (27) P=0.03 Other outcomes Deterioration defined as an increase of 30% or more on the BDI-II Deterioration BDI-II ≥30% increase, 8 weeks, completers (IG1=26; CG=31), N (%) IG1: 1 (3) CG: 0 (0)

Appendix I Table 29. Depression Treatment Studies: Response, Remission, and Loss of Diagnosis (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Wagner et al, 2006 ¹⁵¹	IG1: Escitalopram (N=132) CG: Placebo (N=136)	Response CDRS-R total score ≤28 CGI-I ≤2 CDRS-R response, posttreatment (8 weeks), ITT (IG1=129; CG=132), N (%) IG: 59 (45.7) CG: 50 (37.9) P=0.32 CGI-I response, posttreatment (8 weeks), ITT (IG1=129; CG=132), N (%) IG: 81 (62.8) CG: 69 (52.3) P=0.14

Abbreviations: aOR=adjusted odds ratio; BDI=Beck Depression Inventory; BDI-II=Beck Depression Inventory, version 2; CBT=cognitive behavioral therapy; CDRS-R=Children's Depression Rating Scale-Revised; CES-D=Center for Epidemiological Studies-Depression; CG=control group; CGI=Clinical Global Impressions; CGI-I=Clinical Global Impressions-Improvement; CI=confidence interval; DSM-5=Diagnostic and Statistical Manual of Mental Disorders-5th edition; DSM-III-R=Diagnostic and Statistical Manual of Mental Disorders-3rd edition-Revised; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders-4th edition; HAM-D=Hamilton Depression Rating Scale; IG=intervention group; ITT=intent to treat; KQ=key question; K-SADS=Schedule for Affective Disorders and Schizophrenia for School-Age Children-Early Childhood version; K-SADS-P=Schedule for Affective Disorders and schizophrenia for School-Age Children-Parent; MDD=major depressive disorder; NA=not available; NNT=number needed to treat; NR=not reported; OR=odds ratio; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PHQ-9=Patient Health Questionnaire-9 question; SD=standard deviation; SSRI=selective serotonin reuptake inhibitor; TAU=treatment as usual.

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
Clarke et al, 2016 ⁷⁵ NCT00523081	IG1: CBT + TAU (N=106) CG: TAU (N=106)	CGAS, 52 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 72.33 (9.97) CG: 74.10 (10.81) Effect size: d=0.431; mean difference: 4.2 (95% CI, 1.55 to 6.86) P<0.007 favoring CBT	
		CGAS, 104 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 76.86 (11.03) IG2: 76.45 (11.09) Effect size: d=0.016; mean difference: 0.13 (95% CI, -2.08 to 2.34) P=0.21	
		PEDS-QL, 104 weeks, ITT (IG1=106; CG=106), mean (SD) 52 weeks IG1: 75.40 (14.57) CG: 76.94 (12.43) Effect size: d=0.04; mean difference: 0.55 (95% CI, -3.21 to 4.31) P=0.73	
		PEDS-QL, 104 weeks, ITT (IG1=106; CG=106), mean (SD) IG1: 75.40 (14.57) CG: 76.94 (12.43) Effect size: d=0.09; mean difference: 1.05 (95% CI, -2.27 to 4.36) P=0.90	
Clarke et al, 2005 ⁷⁶ R01-HS10535, HS13854	IG1: Brief CBT + TAU SSRI (N=77) CG: TAU + SSRI (N=75)	IG1: 71.4 (8.7) CG: 68.4 (7.6) Time x Treatment interaction p=0.22, F=1.52 Effect size=0.09; no detectable advantage of CBT SF-12 Mental Component Scale IG1: 45.4 (9.3)	Recurrence of depression among those who had recovered 32 (24%) of 135, N by group NR IG1: 16 (not calculable) CG: 16 (not calculable) Chi squared=0.01, p=0.76, No subgroups of interest
		Time x Treatment interaction p=0.04, F=4.25 Effect size=0.20 favoring CBT condition SF-12 Physical Component Scale IG1: 49.0 (5.8) CG: 48.1 (8.5) Time x Treatment interaction p=0.84, F=0.04 Effect size=0.11; no detectable advantage	reported

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
	IG1: Group CBT (N=45)	GAF, posttreatment (8 weeks), completers (IG1=37; IG2=32; CG=27), mean	
	IG2: Group CBT plus parent	(SD)	
NA	sessions (n=42)	IG1: 71.0 (11.7)	
	CG: Wait-list (N=36)	IG2: 69.9 (14.9)	
		CG: 64.5 (11.8)	
		IG1/IG2 vs. CG: P<0.05; effect size=0.54	
Emslie et al, 200986	IG1: Escitalopram (N=158)	CGAS, change from baseline to 8 weeks, ITT (IG1=154; CG=157), mean	
Findling, 2013 ²²⁷	CG: Placebo (N=158)	difference (SE)	
NCT00107120		IG1: 14.9 (1.11)	
		CG: 12.7 (1.15)	
		LSMD (95% CI): 2.169 (-0.439 to 4.777); P=0.103	
	IG1: PCIT-ED (N=114)	CGAS core score, change from baseline to post assessment, ITT (IG1=114;	
NCT02076425	CG: Wait-list (N=115)	CG=115), adjusted mean difference (SE)	
		-20.5 (2.3)	
		Cohen's d=1.2; P<0.0001	
		PECFAS/CAFAS, change from baseline to post assessment, ITT (IG1=114;	
		CG=115), adjusted mean difference (SE)	
		3.19 (0.46)	
		Cohen's d=0.78; P<0.0001	
		00110113 4-0.70, 1 <0.0001	
		Controlling for baseline characteristics, gender, and baseline externalizing disorder	

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
Registry Number March et al, 2004 ¹¹³	Treatment Interventions and Comparators IG1: Fluoxetine + CBT (N=107) IG2: Fluoxetine + CBT (N=107) IG3: Fluoxetine (N=109) CG: Placebo (N=112)	Functioning Outcomes CGAS, 6 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), unadjusted mean (SD) IG1: 62.4 (11.2) IG2: 59.9 (10.58) IG3: 56.7 (9.66) CG: 57.0 (9.22) CGAS, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), unadjusted mean (SD) IG1: 66.6 (11.91) IG2: 62.1 (11.91) IG3: 60.0 (11.47) CG: 59.3 (12.72) Across 12 weeks time-by-treatment interaction P<0.001; based on linear random coefficient regression, pairwise comparisons IG1 vs. CG: P<0.0001 IG2 vs. CG: P=0.0381 IG3 vs. CG: P=0.3805 CGAS, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112) GLM mean change from baseline (SD) IG1: 16.7 (12.31) IG2: 12.6 (12.31) IG3: 9.7 (12.12) CG: 9.9 (12.38) IG1 vs. CG: P=NS IG3 vs. CG: P=NS	Other Outcomes/ Subgroups
		Rate of nonimpaired patients (CGAS >70), 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), % IG1: 37 (34.6) IG2: 22 (20.2) IG3: 15 (13.5) CG: 21 (18.7) Between-group difference: p=0.002 IG1 vs. CG: P=0.009 IG2 vs. CG: P=NS IG3 vs. CG: P=NS	

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286 (continued)		HoNOSCA, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), unadjusted mean (SD) IG1: 9.5 (5.97) IG2: 10.9 (6.35) IG3: 11.7 (6.09) CG: 11.2 (6.15) Across 12 weeks time-by-treatment interaction P=0.0234; based on linear random coefficient regression, pairwise comparisons IG1 vs. CG: P=0.0393 IG2 vs. CG: p=0.5861 IG3 vs. CG: p=0.3344 HoNOSCA, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), GLM mean change from baseline (SD) IG1: -6.3 (5.69) IG2: -5.1 (5.74) IG3: -3.6 (5.58) CG: -4.2 (5.71) IG1 vs. CG: P=0.01 IG2 vs. CG: P=NS IG3 vs. CG: P=NS	
		PQ-LES-Q, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), unadjusted mean (SD) IG1: 54.7 (11.21) IG2: 51.2 (10.43) IG3: 47.4 (10.84) CG: 48.2 (9.91) Across 12 weeks time-by-treatment interaction P<0.001; based on linear random coefficient regression, pairwise comparisons IG1 vs. CG: P<0.0001 IG2 vs. CG: P=0.7215 IG3 vs. CG: P=0.4630	

Author, Year,	Treatment Interventions	F	Other Outcomes/
Registry Number	and Comparators	Functioning Outcomes	Subgroups
March et al,		PQ-LES-Q, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), GLM mean	
2004 ¹¹³		change from baseline (SD)	
Curry et al, 2006 ²¹⁷		IG1: 9.6 (10.14)	
Emslie et al,		IG2: 6.6 (10.23)	
2006 ²¹⁸		IG3: 4.2 (10.01)	
Kennard et al,		CG: 5.2 (10.16)	
2006 ²¹⁹		IG1 vs. CG: P<0.001	
Vitiello et al,		IG2 vs. CG: P=NS	
2006 ²²⁰		IG3 vs. CG: P=NS	
NCT00006286		IG3: -3.6 (5.58)	
(continued)		CG: -4.2 (5.71)	
		IG1 vs. CG: P<0.01	
		IG2 vs. CG: P=NS	
		IG3 vs. CG: P=NR	
		PQ-LES-Q, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), unadjusted	
		mean (SD)	
		IG1: 54.7 (11.21)	
		IG2: 51.2 (10.43)	
		IG3: 47.4 (10.84)	
		CG: 48.2 (9.91)	
		Across 12 weeks time-by-treatment interaction P<0.001; based on linear	
		random coefficient regression, pairwise comparisons	
		IG1 vs. CG: P<0.0001	
		IG2 vs. CG: P=0.7215	
		IG3 vs. CG: P=0.4630	
		PQ-LES-Q, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), GLM mean	
		change from baseline (SD)	
		IG1: 9.6 (10.14)	
		IG2: 6.6 (10.23)	
		IG3: 4.2 (10.01)	
		CG: 5.2 (10.16)	
		IG1 vs. CG: P<0.001	
		IG2 vs. CG: P=NS	
		IG3 vs. CG: P=NS	

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
Mufson et al, 2004 ¹¹⁸ McGlinchey et al, 2017 ²²⁸	IG1: Interpersonal psychotherapy (N=34) CG: TAU (N=29)	CGAS, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD) IG1: 66.7 (13.0) CG: 59.5 (13.5) P=0.04, effect size=0.54 CGAS, week 16, mITT (IG1=33; CG=29), mean (SD) IG1: NR CG: NR P=0.06, effect size NR SAS-SR Overall, posttreatment (week 12), ITT (IG1=34; CG=29), mean (SD)	
		IG1: 2.23 (0.66) CG: 2.59 (0.67) P=0.01, effect size=0.55 Repeated measures ANOVA Time x Treatment interaction P=0.003	
Richardson et al, 2014 ¹²⁷ NCT01140464	IG1: Collaborative care (N=50) CG: Enhanced usual care (N=51)	CIS, posttreatment (12 months), ITT (IG1=50; CG=51), mean (95% CI) IG1: 16.3 (13.8 to 18.8) CG: 13.4 (10.8 to 15.9) CIS, 6 months, ITT (IG1=50; CG=51), mean difference between groups (95% CI) -4.4 (-8.4 to -0.5), P=0.03 CIS, posttreatment (12 months), ITT (IG1=50; CG=51), m ean difference between groups(95% CI) -4.3 (-8.3 to -0.3), P=0.04	Satisfaction with care (moderately to very satisfied), 6 months, ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 85.8 CG: 52.2 OR (95% CI): 5.6 (1.9 to 16.0), P=0.001 Satisfaction with care (moderately to very satisfied), posttreatment (12 months), ITT (IG1=50; CG=51), imputed % based on 20 multiple imputations IG1: 82.2 CG: 68.5 OR (95% CI): 2.1 (0.7 to 6.1), P=0.001

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
Topooco et al, 2018 ¹⁴⁷ NCT02363205		NR	Deterioration of 30% or more in BDI-II score, completers (IG1=30; CG=36), N (%) IG1: 1 (3) CG: 3 (8) Deterioration of 30% or more in BDI-II score, ITT (IG1=33; CG=37), N (%) IG1: 4 (12) CG: NR
Topooco et al, 2019 ¹⁴⁸ NCT02363205	IG1: Internet CBT (N=35) CG: Attention control (N=35)	NR	Deterioration BDI-II ≥30% increase, 8 weeks, completers (IG1=26; CG=31), N (%) IG1: 1 (3) CG: 0 (0)
Wagner et al, 2006 ¹⁵¹		CGAS, baseline to posttreatment (8 weeks), ITT/LOCF (IG1=129; CG=132), adjusted mean change IG1: 15.6 CG: 12.7 P=0.065	NR

Abbreviations: ANOVA=analysis of variance; BDI-II=Beck Depression Inventory, version 2; CAFAS=Child and Adolescent Functional Assessment Scale; CBT=cognitive behavioral therapy; CG=control group; CGAS=Children's Global Assessment Scale; CI=confidence interval; CIS=Columbia Impairment Scale; GAF=Global Assessment of Functioning; GLM=general linear model; HoNOSCA=Health of the Nation Outcome Scales for Children and Adolescents; ITT=intent to treat; KQ=key question; LOCF=last observation carried forward; LSMD=least-square mean difference; mITT=modified intent to treat; NA=not available; NR=not reported; NS=not significant; OR=odds ratio; PCIT-ED=Parent Child Interaction Therapy-Emotion Development; PECFAS= Preschool and Early Childhood Functional Assessment Scale/Child and Adolescent Functional Assessment Scale; PEDS-QL= Pediatric Quality of Life Inventory; PQ-LES-Q=Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire; SAS-SR=Social Adjustment Scale-Self Report; SD=standard deviation; SE=standard error; SF-12=Short Form-12; SSRI=selective serotonin reuptake inhibitor; TAU=treatment as usual.

Appendix I Table 31. Depression Treatment Studies: Suicide-Related Harms and Suicide-Related Withdrawal (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Suicide-Related Symptoms
Clarke et al, 2016 ⁷⁵ NCT00523081	IG1: CBT + TAU (N=106) CG: TAU (N=106)	K-SADS suicidal behavior, 52 weeks, ITT (IG1=106; CG=106), n (%) IG1: 5 (5.8) CG: 2 (2.4) Effect size NNT=37, OR: 1.03 (95% CI, 0.47 to 2.27) P=0.27 K-SADS suicidal behavior, 104 weeks, ITT (IG1=106; CG=106), n (%) IG1: 1 (1.1) CG: 1 (1.1) Effect size NNT=11, OR: 1.21 (95% CI, 0.32 to 3.78)
Emslie et al, 2009 ⁸⁶ Findling, 2013 ²²⁷ NCT00107120	IG1: Escitalopram (N=158) CG: Placebo (N=158)	P=0.51 Self-harm related AE (other than suicidality), baseline to 8 weeks, ITT (IG1=155; CG=157), N (%) IG1: 6 (3.9) CG: 6 (3.8) See efficacy section for additional measures related to suicidality IG: 0 CG: 1 (withdrawal from study for insufficient therapeutic response and initiation of commercially available escitalopram)
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	IG1: Fluoxetine + CBT (N=107) IG2: Fluoxetine + CBT (N=107) IG3: Fluoxetine (N=109) CG: Placebo (N=112)	See suicide outcomes in efficacy section for SIQ-Jr scores Suicide-related AEs, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), N (%) IG1: 6 (5.61) reported in March et al; 5 (4.7%) reported in Emslie et al IG2: 9 (8.26) reported in March et al; 10 (9.2%) reported in Emslie et al IG3: 5 (4.50) CG: 4 (3.57) reported in March et al; 3 (5.2%) reported in Emslie et al Suicide-related AEs, OR (95% CI) vs. CG IG1: 1.6 (0.44 to 5.85) IG2: 2.4 (0.73 to 8.14) IG3: 1.3 (0.33 to 4.87) CG: NA Suicide attempts, ITT (IG1=107; IG2=109; IG3=111; CG=112), N (calculated %) IG1: 2 (1.9%) reported in Emslie et al; 4 (3.7%) reported in March et al IG2: 2 (1.83%) IG3: 1 (0.90%) CG: 0 N of events too small to allow statistical comparison of suicide events No completed suicides

Appendix I Table 31. Depression Treatment Studies: Suicide-Related Harms and Suicide-Related Withdrawal (KQ 5)

Author, Year, Registry	Treatment Interventions and	
Number	Comparators	Suicide-Related Symptoms
,		Potential suicide-related events, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 1 (7.8)
	,	CG: 2 (1.5)
		Withdrawal due to suicidal ideation, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 0 (0) CG: 0 (0)

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; IG=intervention group; ITT=intent to treat; KQ=key question; K-SADS=Schedule for Affective Disorders and schizophrenia for School-Age Children; NA=not available; NNT=number needed to treat; OR=odds ratio; SIQ=Suicidal Ideation Questionnaire; TAU=treatment as usual.

Appendix I Table 32. Depression Treatment Studies: Harms (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal Due to AE	Other Harms
Emslie et al, 2009 ⁸⁶ Findling, 2013 ²²⁷ NCT00107120	IG1: Escitalopram (N=158) CG: Placebo (N=158)	Total adverse events, baseline to 8 weeks, safety population (IG=155; CG=157), N (%) IG1: 121 (78.1) CG: 118 (75.2)	SAEs, baseline to 8 weeks, safety population (IG1=155; CG=157), N (%) IG1: 4 (2.6) (1 sexual assault, 1 self-injurious behavior, 1 suicidal ideation, 1 irritability) CG: 2 (1.3) (1 suicidal tendency, 1 aggravated depression)	Discontinued due to AEs, baseline to 8 weeks, safety population (IG1=155; CG=157), N (%) IG1: 4 (2.6) CG: 1 (0.6) P=0.21 IG: 0 CG: 1 (withdrawal from study for insufficient therapeutic response and initiation of commercially available escitalopram)	NR
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286	IG1: Fluoxetine + CBT (N=107) IG2: Fluoxetine + CBT (N=107) IG3: Fluoxetine (N=109) CG: Placebo (N=112)	Physical AEs requiring medical attention or causing dysfunction, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), N patients [N events] (%) IG1: 37 [61] (34.5) IG2: 35 [81] (32.1) IG3: 9 [NR] (8.1) CG: 34 [60] (30.4) Any psychiatric-related AEs, 12 weeks (posttreatment), ITT (IG1=107; IG2=109; IG3=111; CG=112), N patients [N events] (%) IG1: 12 [16] (15) IG2: 20 [23] (21) IG3: 1 [1] (1) CG: 9 [11] (9.8)	Serious AEs, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), N (%) IG1: 9 (8.41) IG2: 13 (11.93) IG3: 5 (4.50) CG: 6 (5.36) Serious AEs, OR (95% CI) vs. CG: IG1: 1.6 (0.56 to 4.72) IG2: 2.4 (0.87 to 6.54) IG3: 0.8 (0.25 to 2.81) CG: NA Between-group P=0.15 NOTE: ORs ≤2 reflect little or no increased risk	NR	NR

Appendix I Table 32. Depression Treatment Studies: Harms (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal Due to AE	Other Harms
March et al, 2004 ¹¹³ Curry et al, 2006 ²¹⁷ Emslie et al, 2006 ²¹⁸ Kennard et al, 2006 ²¹⁹ Vitiello et al, 2006 ²²⁰ NCT00006286 (continued)			Serious psychiatric-related AEs, 12 weeks, ITT (IG1=107; IG2=109; IG3=111; CG=112), N patients [N events], (calculated %) IG1: 0 IG2: 1 [1] (0.92) (worsening depression, also captured below) IG3: 0 CG: 1 [1] (0.89) (mania, also captured below) These events more frequent in fluoxetine arms (IG1 and IG2) than CBT (IG3) or placebo (CG), but P=NR		
Richardson et al, 2014 ¹²⁷ NCT01140464	IG1: Collaborative care (N=50) CG: Enhanced usual care (N=51)	NR	NR	NR	Psychiatric Hospitalization, ITT (IG1=50; CG=51), N(%) IG: 3 (6) CG: 2 (4) Emergency Department Visit with a Primary Psychiatric Diagnosis, ITT (IG1=50; CG=51), N(%) IG: 1 (2) CG: 5 (10)

Appendix I Table 32. Depression Treatment Studies: Harms (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Incidence Any AEs	Incidence of SAEs	Withdrawal Due to AE	Other Harms
Wagner et al, 2006 ¹⁵¹	IG1: Escitalopram (N=132) CG: Placebo (N=136)	Any AE, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 90 (68.7) CG: 90 (67.7) P=0.90	Any SAE, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 2 (1.5), pneumonia, accidental injury CG: 3 (2.3) (allergic reaction, manic reaction, worsening depression)	Withdrawal due to any AE, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 2 (1.5) CG: 2 (1.5) Withdrawal due to suicidal ideation, posttreatment (8 weeks), safety (IG1=131; CG=133), N (%) IG1: 0 (0) CG: 0 (0)	NR

Abbreviations: AE=adverse event; CBT=cognitive behavioral therapy; CG=control group; CI=confidence interval; IG=intervention group; ITT=intent to treat KQ=key question; NA=not available; NR=not reported; OR=odds ratio; SAE=serious adverse event.

Appendix I Table 33. Depression Studies: Characteristics of Systematic Reviews, Meta-Analyses, or Network Meta-Analyses (KQ 5)

Author,	Study	Search Dates		
Year	Design	Covered	Study Selection Criteria	Included Studies (Participants)
Cipriani et al, 2016 ¹⁶¹	Network meta- analysis	Database inception through May 3015	 Double-blind RCTs comparing any antidepressant with placebo or another antidepressant as oral therapy for the acute treatment of children and adolescents with MDD, without restrictions on language. Eligible medications (as long as administered within the therapeutic dose range) included amitriptyline, citalopram, clomipramine, desipramine, duloxetine, escitalopram, fluoxetine, imipramine, mirtazapine, nefazodone, nortriptyline, paroxetine, sertraline, and venlafaxine. Studies were excluded if they focused on treatment-resistant depression, had a duration less than 4 weeks, or had fewer than 10 patients. 	34 RCTs (5,260) Mean (range) sample size: 159 (23 to 463) % Female: 53 Mean (SD) age: 13.6 (2.87) Median (range) duration of treatment: 8 weeks (5 to 12) % conducted in North America: 50 % high risk of bias: 29 % moderate risk of bias: 59 % low risk of bias: 12

Abbreviations: KQ=key question; MDD=major depressive disorder; RCT=randomized controlled trial; SD=standard deviation.

Appendix I Table 34. Depression Studies: Results of Systematic Reviews, Meta-Analyses, or Network Meta-Analyses (KQ 5)

Author, Year	Adverse Event Findings	Suicidality Findings
Cipriani et al,	Discontinuations due to AEs, OR (95% CI)	Suicide behavior or ideation (measures not specified)
2016 ¹⁶¹	Clomipramine vs. placebo: 1.01 (0.43 to 2.38)	Clomipramine vs. placebo: 0.82 (0.29 to 2.38)
2010	Duloxetine vs. placebo: 2.75 (1.18 to 6.44)	Duloxetine vs. placebo: 0.90 (0.55 to 1.48)
	Escitalopram vs. placebo: 1.90 (0.44 to 8.28)	Escitalopram vs. placebo: 0.99 (0.47 to 2.08)
	Fluoxetine vs. placebo: 1.09 (0.44 to 2.72)	Fluoxetine vs. placebo: 1.12 (0.72 to 1.73)
	Sertraline vs. placebo: 3.60 (1.40 to 10.63)	Sertraline vs. placebo: 1.92 (0.33 to 11.06)
		Surface under the cumulative ranking curve (larger values indicate safer
	more tolerable medications)	interventions with respect to suicide behavior or ideation)
	Placebo: 82.5%	Placebo: 65.6%
	Fluoxetine: 75.7%	Duloxetine: 65.3%
	Clomipramine: 57.2%	Escitalopram: 60.4%
	Escitalopram: 47.3%	Clomipramine: 59.7%
	Duloxetine: 33.9%	Fluoxetine: 53.3%
	Sertraline: 29.6%	Sertraline: 28.0%

Abbreviations: AE=adverse event; CI=confidence interval; KQ=key question; MDD=major depressive disorder; OR=odds ratio; RCT=randomized, controlled trial; SD=standard deviation.

Appendix I Table 35. Anxiety or Depression Treatment Studies: Study Characteristics (KQ 4 & KQ 5)

Author, Year Registry Number	Country Study Design Funding	Setting	Intervention(s)	Comparator	Quality
Ehrenreich-May et al, 2017 ⁸⁴	U.S. RCT National Institute of Mental Health	Potential participants and their parents were referred to the clinic by teachers, school counselors, pediatricians, psychiatrists, other mental health and health care professionals, or were self-referred through	IG1: UP-A (N=27)	CG: Wait-list (N=24) Delayed treatment wait-list lasting	Some concerns
Weersing et al, 2017 ¹⁵⁶ Brent et al, 2019 ²²⁹ NCT01147614	U.S. RCT National Institute of Mental Health	Nine pediatric primary care settings in San Diego and Pittsburgh. Participants were clinically referred by pediatrics staff or self-referred from flyers in practices.	IG1: Brief behavioral therapy (N=95) Description: 8 to 12 weekly 45-minute sessions completed over 16 weeks. Exposure and behavioral activation were combined through graded engagement in avoided activities and supplemented by relaxation to manage somatic symptoms and problem-solving skills to aid in stress management. Duration: 16 weeks	CG: Assisted referral (N=90) Participants in the assisted referral condition received feedback about symptoms and benefits of services, referrals, and education about obtaining services and problems-solving barriers to treatment. The study coordinator contacted the youth's primary caregiver at least every 2 weeks during the acute treatment phase to check in and problem solve obstacles to care. ARC coordinators connected 82.2% of families with specialty mental health care for a mean of 6.5 outpatient sessions.	Some concerns

Abbreviations: ARC=assisted referral to care; CG=control group; IG=intervention group; KQ=key question; RCT=randomized, controlled trial; UP-A=Unified Protocol for the Treatment of Emotional Disorders in Adolescents.

	Patient Characteristics:			
A 41 - 14 - 15 - 14	Age, Mean (SD)			
Author, Year, Registry Number	Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
	Mean age (SD): 15.77 (1.66)	Ages 12 to 17 years with a	Bipolar disorder, recent	Principal diagnosis %
2017 ⁸⁴			psychiatric hospitalization or	Generalized anxiety disorder: 41.2%
	N (%) Female: 29 (56.9)	DSM-IV anxiety disorder	severe suicidal ideation,	Social phobia: 31.4%
	.		significant cognitive	Major depressive disorder: 21.6%
	Race/Ethnicity:	compulsive disorder) and/or	Impairment (suspected IQ below 80), or with treatment-	Obsessive compulsive disorder: 5.9%
	Hispanic/Latino: 30 (59) Non-Hispanic White: 12 (24)		interfering substance abuse.	Anxiety disorder, NOS: 5.9% Panic disorder without agoraphobia:
	African American: 4 (8)		Had previously received CBT	3.9%
	Asian American: 1 (2)		for anxiety or depression.	Specific phobia: 3.9%
	Other: 4 (8)	on a stable dosage of an		Dysthymic disorder: 3.9%
		SSRI for 3 months, or 1		Posttraumatic stress disorder: 3.9%
		month for a benzodiazepine,		Panic disorder with agoraphobia: 2.9%
		prior to enrolling in the study.		Depressive disorder, NOS: 2.9% Trichotillomania: 2%
		Study.		Comorbid diagnosis %
				Generalized anxiety disorder: 27.5%
				Social phobia: 19.6%
				Major depressive disorder: 29.4%
				Obsessive compulsive disorder: 7.8%
				Anxiety disorder, NOS: 17.6% Panic disorder without agoraphobia:
				3.9%
				Specific phobia: 21.6%
				Dysthymic disorder: 3.9%
				Posttraumatic stress disorder: 2%
				Depressive disorder, NOS: 15.7%
				Trichotillomania: 2%
				Attention deficit/hyperactivity disorder: 15.7%
				Separation anxiety disorder: 2%
				Eating disorder, NOS: 2%
				Learning disorder: 2% Substance-related disorder: 2%
				Communication disorder: 2%

Appendix I Table 36. Anxiety or Depression Treatment Studies: Population Characteristics (KQ 4 & KQ 5)

Author, Year, Registry Number	Patient Characteristics: Age, Mean (SD) Female, N (%) Race/Ethnicity	Inclusion Criteria	Exclusion Criteria	Prevalence of Psychiatric/ Behavioral Conditions
	Mean age (SD): 11.3 (2.6)	Ages 8 to 16 years meeting		Primary/target condition
Brent et al, 2019 ²²⁹				One or more anxiety disorders: 62%
	N (%) Female: 107 (57.8)	probable diagnoses of SepAD, GAD, SocAD, MDD,	current suicidal plan, bipolar disorder, psychosis, PTSD,	Anxiety and clinically elevated depression: 32%
	Race/Ethnicity:	dysthymic disorder, or minor	substance dependence,	Clinically significant depression without
	White: 144 (77.8)	depression and living with a	current abuse, intellectual	anxiety: 6%
	Hispanic: 38 (20.7)	consenting legal guardian	disability, school placement	
		for at least 6 months.	below 2nd grade, or unstable	
			serious physical illness	

Abbreviations: CBT=cognitive behavioral therapy; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; GAD=generalized anxiety disorder; IQ=intelligence quotient; KQ=key question; MDD=major depressive disorder; NOS=not otherwise specified; PTSD=post-traumatic stress disorder; SD=standard deviation; SepAD=separation anxiety disorder; SocAD=social anxiety disorder; SSRI=selective serotonin reuptake inhibitor.

Appendix I Table 37. Anxiety or Depression Treatment Studies: Anxiety-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Anxiety Symptoms
	IG1: UP-A (N=27) CG: Wait-list (N=24)	Principal diagnosis ADIS CSR, 8 weeks, ITT (IG1=21; CG=16), mean (SD) IG1: 4.1 (1.53) CG: 5.4 (1.27) Time x Treatment interaction P<0.006
		CGI-Severity, ITT, (IG1=21; CG=16), mean (SD) IG1: 4.1 (1.31)
		CG: 5.1 (1.02) Time x Treatment interaction P<0.006
		CGI-Improvement, ITT, (IG1=21; CG=16), mean IG1: 3.04 CG: 4.00 t(36)=2.55, p=0.016, d=0.85
	CG: Assisted referral (N=90)	CGI-I, posttreatment 16 weeks, ITT (IG=95; CG=90), mean (SD) IG1: 2.3 (1.1) CG: 3.1 (1.3)
		CGI-S, posttreatment 16 weeks, ITT (IG=95; CG=90), mean (SD) IG1: 2.6 (1.2) CG: 3.4 (1.3)
		PARS, posttreatment 16 weeks, ITT (IG=95; CG=90), mean (SD) IG1: 8.6 (5.0) CG: 11.4 (6.4)
		Treatment x Time P=0.01, Cohen's f=0.28 PARS, 32 weeks, ITT (IG=95; CG=90), mean (SD) IG1: NR
		CG: NR Treatment x Time P=0.003, Cohen's f=0.21

Abbreviations: ADIS=Anxiety Disorders Interview Schedule; CG=control group; CGI=Clinical Global Impressions; CGI-I=Clinical Global Impressions-Improvement; CGI-S=Clinical Global Impressions-Severity; CSR=Clinician Severity Ratings; IG=intervention group; ITT=intent to treat; KQ=key question; NR=not reported; PARS=Pediatric Anxiety Rating Scale; SD=standard deviation; UP-A=Unified Protocol for the Treatment of Emotional Disorders in Adolescents.

Appendix I Table 38. Anxiety or Depression Treatment Studies: Depression-Related Outcomes (KQ 4)

Author, Year, Registry Number	Treatment Interventions and Comparators	Depression Symptoms
,	IG1: UP-A (N=27) CG: Wait-list (N=24)	RCADS, 8 weeks, ITT (IG1=21; CG=16), mean (SD) IG1: 105.9 (29.51) CG: 102.5 (27.53) Time v. Tractment interaction D: 0.40
		Time x Treatment interaction P>0.40 RCADS-P, 8 weeks, ITT (IG1=21; CG=16), mean (SD) IG1: 130.3 (24.68) CG: 129.8 (23.32) Time x Treatment interaction P>0.40
	IG1: Brief behavioral therapy (N=95) CG: Assisted referral (N=90)	CDRS-R, posttreatment 16 weeks, ITT (IG=95; CG=90), mean (SD) IG1: 22.6 (7.3) CG: 25.2 (9.4) Treatment x Time P=0.38, Cohen's f=0.07
		CDRS-R, 32 weeks, ITT (IG=95; CG=90), mean (SD) IG1: NR CG: NR Treatment x Time P=0.64, Cohen's f=0.05

Abbreviations: CDRS-R=Children's Depression Rating Scale-Revised; CG=control group; IG=intervention group; ITT=intent to treat; KQ=key question; NR=not reported; RCADS=Revised Children's Anxiety and Depression Scale-Parent; SD=standard deviation; UP-A=Unified Protocol for the Treatment of Emotional Disorders in Adolescents.

Appendix I Table 39. Anxiety or Depression Treatment Studies: Response, Remission, and Loss of Diagnosis Outcomes (KQ 5)

Author, Year, Registry Number	Treatment Interventions and Comparators	Response Remission Loss of Diagnosis
Weersing et al, 2017 ¹⁵⁶ Brent et al, 2019 ²²⁹ NCT01147614	IG1: Brief behavioral therapy (N=95) CG: Assisted referral (N=90)	Response CGI-I scores ≤2 for anxiety and depression CGI-I ≤2, posttreatment (16 weeks), completers (IG1=88; CG=71), N (%) IG1: 50 (56.8) CG: 20 (28.2) P<0.001 CGI-I ≤2, 32 weeks, ITT (IG1=95; CG=90), N (%) IG1: NR (67.5) CG: NR (43.1) P=0.002 Remission CGI-I score=1 for anxiety and depression CGI-I score=1, 32 weeks, ITT (IG1=95; CG=90), N (%) IG: NR (36.3) CG: NR (22.2) P=0.06 Loss of diagnosis NR Other outcomes NR

Abbreviations: CG=control group; CGI-I=Clinical Global Impressions-Improvement; IG=intervention group; ITT=intent to treat; KQ=key question; NR=not reported.

Author, Year, Registry Number	Treatment Interventions and Comparators	Functioning Outcomes	Other Outcomes/ Subgroups
Ehrenreich-May	IG1: UP-A (N=27)	ALIS, 8 weeks, ITT (IG1=21; CG=16), mean (SD)	Ethnicity moderated response, with
et al, 2017 ⁸⁴	CG: Wait-list (N=24)	IG1: 28.2 (24.18)	Hispanic youths having a
		CG: 37.3 (27.31)	heightened response and greater
		Time x Treatment interaction P>0.40	improvements in functioning
Weersing et al, 2017 ¹⁵⁶	(N=95)	CGAS, posttreatment 16 weeks, ITT (IG=95; CG=90), mean (SD) IG1: 68.5 (10.7)	No subgroups of interest reported
Brent et al,	` ,	CG: 61.9 (11.9)	
2019 ²²⁹		Time x Treatment P=0.001, Cohen's d=0.58	
		CGAS, 32 weeks, ITT (IG=95; CG=90), mean (SD)	
		IG1: 70.9 (11.4)	
		CG: 65.0 (13.1)	
		Time x Treatment P=0.004, Cohen's d=0.49	

Abbreviations: ALIS= adolescent life interference scale; CG=control group; CGAS=Children's Global Assessment Scale; IG=intervention group; ITT=intent to treat; KQ=key question; SD=standard deviation; UP-A=Unified Protocol for the Treatment of Emotional Disorders in Adolescents.

List of Exclusion Codes:

X1: Non-English

X2: Ineligible population

X3: Ineligible intervention

X4: Ineligible comparator

X5: Ineligible setting

X6: Ineligible country

X7: Ineligible study design

X8: Ineligible publication type

X9: Ineligible outcome

X10: Duplicate

X11: Relevant protocol or ongoing study

X12: Superseded by full publication

X13: Poor quality

- Fluvoxamine for the treatment of anxiety disorders in children and adolescents. The Research Unit on Pediatric Psychopharmacology Anxiety Study Group. N Engl J Med. 2001 Apr 26;344(17):1279-85. doi: 10.1056/nejm200104263441703. PMID: 11323729. Exclusion Code: X10.
- Children with anxiety do best on combination therapy. Drug Benefit Trends. 2008;20(12):504-. PMID: 2008-19322-002. Exclusion Code: X8.
- 3. Corrections: (The Lancet Psychiatry (2017) 4 (2)(109-119) (S2215036616303789) (10.1016/S2215-0366(16)30378-9)). The lancet psychiatry. 2017;4(8):582. doi: 10.1016/S2215-0366%2817%2930283-3. PMID: CN-01475235. Exclusion Code: X4.
- 4. Re: "Desvenlafaxine versus placebo in a Fluoxetine-referenced study of children and adolescents with major depressive disorder: design, definitions, and ongoing challenges for child and adolescent psychopharmacology research" by Strawn JR and Croarkin PE (J Child Adolesc Psychopharmacol 2018;28: (5)363). J Child Adolesc Psychopharmacol. 2019;29(3):245-6. doi: 10.1089/cap.2018.0163. PMID: CN-02001995. Exclusion Code: X2.
- 5. 5.4 Tailoring treatment over time: a clinical trial using measurement-based care within an integrated care pathway. J Am Acad Child Adolesc Psychiatry. 2020;59(10):S274-. doi:

- 10.1016/j.jaac.2020.07.575. PMID: CN-02207475. Exclusion Code: X9.
- Changes in firearm and medication storage practices in homes of youths at risk for suicide: results of the SAFETY Study, a clustered, emergency department—based, multisite, steppedwedge trial. Ann Emerg Med. 2020doi: 10.1016/j.annemergmed.2020.02.007. PMID: CN-02147046. Exclusion Code: X2.
- Aalsma MC, Zerr AM, Etter DJ, et al. Physician intervention to positive depression screens among adolescents in primary care. J Adolesc Health. 2018 Feb;62(2):212-8. doi: 10.1016/j.jadohealth.2017.08.023. PMID: 29174939. Exclusion Code: X7.
- 8. Ab Ghaffar SF, Mohd Sidik S, Ibrahim N, et al. Effect of a school-based anxiety prevention program among primary school children. Int J Environ Res Public Health. 2019 Dec 5;16(24)doi: 10.3390/ijerph16244913. PMID: 31817328. Exclusion Code: X2.
- Abbasi Z, Amiri S, Talebi H. The effective comparison between modular cognitive behavioral therapy (MCBT) and child-parent relationship training (CPRT) in children with separation anxiety symptoms. Social Sciences (Pakistan). 2016;11(6):890-902. Exclusion Code: X6.
- 10. Abotsie G, Cestaro V, Gee B, et al. Interpersonal counselling for adolescent depression delivered by youth mental health workers without core

- professional training: a feasibility randomised controlled trial study protocol. Pilot Feasibility Stud. 2020 Dec 10;6(1):191. doi: 10.1186/s40814-020-00733-8. PMID: 33298193. Exclusion Code: X2.
- 11. Adler Nevo GW, Avery D, Fiksenbaum L, et al. Eight years later: outcomes of CBT-treated versus untreated anxious children. Brain Behav. 2014 Sep;4(5):765-74. doi: 10.1002/brb3.274. PMID: 25328851. Exclusion Code: X7.
- 12. Afshari A, Neshat-Doost HT, Maracy MR, et al. The effective comparison between emotion-focused cognitive behavioral group therapy and cognitive behavioral group therapy in children with separation anxiety disorder. J Res Med Sci. 2014 Mar;19(3):221-7. PMID: 24949029. Exclusion Code: X6.
- Aguinaldo LD, Sullivant S, Lanzillo EC, et al. Validation of the ask suicide-screening questions (ASQ) with youth in outpatient specialty and primary care clinics. Gen Hosp Psychiatry. 2021 Jan-Feb;68:52-8. doi: 10.1016/j.genhosppsych.2020.11.006. PMID: 33310014. Exclusion Code: X4.
- Ahmadi A, Mustaffa MS, Haghdoost AA, et al. Eclectic approach to anxiety disorders among rural children. Trends Psychiatry Psychother. 2017 Apr-Jun;39(2):88-97. doi: 10.1590/2237-6089-2016-0047. PMID: 28700038. Exclusion Code: X2.
- 15. Ahmed N, John A, Islam S, et al. Investigating the feasibility of an enhanced contact intervention in self-harm and suicidal behaviour: a protocol for a randomised controlled trial delivering a Social support and Wellbeing Intervention following Self Harm (SWISH). BMJ Open. 2016 Sep 14;6(9):e012043. doi: 10.1136/bmjopen-2016-012043. PMID: 27630071. Exclusion Code:
- 16. Alavi A, Sharifi B, Ghanizadeh A, et al. Effectiveness of cognitive-behavioral therapy in decreasing suicidal ideation and hopelessness of the adolescents with previous suicidal attempts. Iran J Pediatr. 2013 Aug;23(4):467-72. PMID: 24427502. Exclusion Code: X6.
- 17. Alcázar AIR, Olivares-Olivares PJ, Rodríguez JO. The role of non-specific effects in the psychological treatment of adolescents with social phobia. Anuario de Psicología/The UB Journal of Psychology. 2009;40(1):43-61. Exclusion Code: X1.
- Alfano CA, Ginsburg GS, Kingery JN. Sleeprelated problems among children and adolescents with anxiety disorders. J Am Acad Child Adolesc Psychiatry. 2007;46(2):224-32. doi: 10.1097/01.chi.0000242233.06011.8e. PMID: 2007-01344-010. Exclusion Code: X9.
- 19. Allen JL, Blatter-Meunier J, Ursprung A, et al. The separation anxiety daily diary: child version: feasibility and psychometric properties. Child Psychiatry Hum Dev. 2010;41(6):649-62. doi:

- 10.1007/s10578-010-0194-1. PMID: 2010-21825-006. Exclusion Code: X7.
- Allen JL, Blatter-Meunier J, Ursprung A, et al. Maternal daily diary report in the assessment of childhood separation anxiety. J Clin Child Adolesc Psychol. 2010;39(2):252-9. doi: 10.1080/15374410903532619. PMID: 2010-07582-010. Exclusion Code: X9.
- 21. Amir N, Beard C, Taylor CT, et al. Attention training in individuals with generalized social phobia: A randomized controlled trial. J Consult Clin Psychol. 2009 Oct;77(5):961-73. doi: 10.1037/a0016685. PMID: 19803575. Exclusion Code: X3.
- Amoros-Boix M R-AA, Olivares-Olivares PJ.
 Role of the focus of attention in the treatment of generalized social phobia in adolescents. Anales
 De Psicologia. 2011;27(3). Exclusion Code: X1.
- 23. Angold A, Erkanli A, Copeland W, et al. Psychiatric diagnostic interviews for children and adolescents: a comparative study. J Am Acad Child Adolesc Psychiatry. 2012 May;51(5):506-17. doi: 10.1016/j.jaac.2012.02.020. PMID: 22525957. Exclusion Code: X4.
- 24. Apsche JA, Bass CK, Houston M-A. A one year study of adolescent males with aggression and problems of conduct and personality: A comparison of MDT and DBT. International Journal of Behavioral Consultation and Therapy. 2006;2(4):544. Exclusion Code: X2.
- Apter A. Adolescent self-harm: New horizons? J Am Acad Child Adolesc Psychiatry.
 2014;53(10):1048-9. doi: 10.1016/j.jaac.2014.07.011. PMID: 2014-41032-008. Exclusion Code: X7.
- Arándiga AV, Rodríguez, et al. Competencia social y autoestima en adolescentes con fobia social. . Investigar el cambio curricular en el espacio europeo de educación superior. . 2014:459-79. Exclusion Code: X1.
- 27. Archer J. Randomised controlled trial: collaborative care improves clinical outcomes for adolescents with depression treated in primary care. Evid Based Med. 2015;20(1):20. doi: 10.1136/ebmed-2014-110108. PMID: CN-01072499. Exclusion Code: X8.
- 28. Armitage CJ, Rahim WA, Rowe R, et al. An exploratory randomised trial of a simple, brief psychological intervention to reduce subsequent suicidal ideation and behaviour in patients admitted to hospital for self-harm. Br J Psychiatry. 2016 May;208(5):470-6. doi: 10.1192/bjp.bp.114.162495. PMID: 26743808. Exclusion Code: X2.
- Asarnow JR. Depression in childhood: one year outcomes of family versus individual treatment. J Am Acad Child Adolesc Psychiatry. 2018;57(10):S289-S90. doi: 10.1016/j.jaac.2018.07.692. PMID: CN-01653013. Exclusion Code: X12.
- 30. Asarnow JR, Berk M, Bedics J, et al. Dialectical behavior therapy for suicidal self-harming

- youths: emotion regulation, mechanisms, and mediators. J Am Acad Child Adolesc Psychiatry. 2021doi: 10.1016/j.jaac.2021.01.016. PMID: CN-02245272. Exclusion Code:
- 31. Asarnow JR, Berk MS, Bedics J, et al. Dialectical behavior therapy for suicidal self-harming youth: emotion regulation, mechanisms, and mediators. J Am Acad Child Adolesc Psychiatry. 2021 Feb 1doi: 10.1016/j.jaac.2021.01.016. PMID: 33539915. Exclusion Code: X4.
- 32. Asarnow JR, Emslie G, Clarke G, et al.
 Treatment of selective serotonin reuptake
 inhibitor-resistant depression in adolescents:
 predictors and moderators of treatment response.
 J Am Acad Child Adolesc Psychiatry. 2009
 Mar;48(3):330-9. doi:
 10.1097/CHI.0b013e3181977476. PMID:
 19182688. Exclusion Code: X2.
- Asarnow JR, Jaycox LH, Duan N, et al.
 Effectiveness of a quality improvement
 intervention for adolescent depression in primary
 care clinics: a randomized controlled trial.
 JAMA. 2005 Jan 19;293(3):311-9. doi:
 10.1001/jama.293.3.311. PMID: 15657324.
 Exclusion Code: X2.
- 34. Asarnow JR, Jaycox LH, Tang L, et al. Longterm benefits of short-term quality improvement interventions for depressed youths in primary care. Am J Psychiatry. 2009 Sep;166(9):1002-10. doi: 10.1176/appi.ajp.2009.08121909. PMID: 19651711. Exclusion Code: X5.
- 35. Atkinson S, Thurman L, Ramaker S, et al. Safety, tolerability, and efficacy of desvenlafaxine in children and adolescents with major depressive disorder: results from two open-label extension trials. CNS Spectr. 2019 Oct;24(5):496-506. doi: 10.1017/s1092852918001128. PMID: 30419989. Exclusion Code: X4.
- 36. Atkinson SD, Prakash A, Zhang Q, et al. A double-blind efficacy and safety study of duloxetine flexible dosing in children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2014 May;24(4):180-9. doi: 10.1089/cap.2013.0146. PMID: 24813026. Exclusion Code: X13.
- 37. Azadeh SM, Kazemi-Zahrani H, Besharat MA. Effectiveness of acceptance and commitment therapy on interpersonal problems and psychological flexibility in female high school students with social anxiety disorder. Glob J Health Sci. 2015 Jul 12;8(3):131-8. doi: 10.5539/gjhs.v8n3p131. PMID: 26493425. Exclusion Code: X6.
- 38. Azzopardi C, Greenblatt A, Korczak DJ, et al. Pediatric hospital screening for suicide risk in adolescents referred for maltreatment. Child Youth Serv Rev. 2020;119doi: 10.1016/j.childyouth.2020.105500. PMID: 2020-97548-001. Exclusion Code: X2.
- Babeva KN, Klomhaus AM, Sugar CA, et al. Adolescent suicide attempt prevention: predictors of response to a cognitive-behavioral family and

- youth centered intervention. Suicide Life Threat Behav. 2020 Feb;50(1):56-71. doi: 10.1111/sltb.12573. PMID: 31350782. Exclusion Code: X7
- 40. Baer S, Garland EJ. Pilot study of community-based cognitive behavioral group therapy for adolescents with social phobia. J Am Acad Child Adolesc Psychiatry. 2005 Mar;44(3):258-64. doi: 10.1097/00004583-200503000-00010. PMID: 15725970. Exclusion Code: X13.
- 41. Baldofski S, Kohls E, Bauer S, et al. Efficacy and cost-effectiveness of two online interventions for children and adolescents at risk for depression (E.motion trial): study protocol for a randomized controlled trial within the ProHEAD consortium. Trials. 2019 Jan 15;20(1):53. doi: 10.1186/s13063-018-3156-8. PMID: 30646944. Exclusion Code: X2.
- 42. Ballard ED, Cwik M, Van Eck K, et al. Identification of at-risk youth by suicide screening in a pediatric emergency department. Prev Sci. 2017 Feb;18(2):174-82. doi: 10.1007/s11121-016-0717-5. PMID: 27678381. Exclusion Code: X2.
- 43. Ballard ED, Snider SL, Nugent AC, et al. Active suicidal ideation during clinical antidepressant trials. Psychiatry Res. 2017 Nov;257:303-8. doi: 10.1016/j.psychres.2017.07.065. PMID: 28787656. Exclusion Code: X2.
- 44. Bansa M, Brown D, DeFrino D, et al. A little effort can withstand the hardship: fielding an internet-based intervention to prevent depression among urban racial/ethnic minority adolescents in a primary care setting. J Natl Med Assoc. 2018 Apr;110(2):130-42. doi: 10.1016/j.jnma.2017.02.006. PMID: 29580446. Exclusion Code: X2.
- 45. Barbe RP, Bridge J, Birmaher B, et al. Suicidality and its relationship to treatment outcome in depressed adolescents. Suicide Life Threat Behav. 2004 Spring;34(1):44-55. PMID: 15106887. Exclusion Code: X4.
- 46. Barbe RP, Bridge JA, Birmaher B, et al. Lifetime history of sexual abuse, clinical presentation, and outcome in a clinical trial for adolescent depression. J Clin Psychiatry. 2004 Jan;65(1):77-83. PMID: 14744173. Exclusion Code: X4.
- 47. Barch DM, Whalen D, Gilbert K, et al. Neural indicators of anhedonia: predictors and mechanisms of treatment change in a randomized clinical trial in early childhood depression. Biol Psychiatry. 2019 May 15;85(10):863-71. doi: 10.1016/j.biopsych.2018.11.021. PMID: 30583852. Exclusion Code: X9.
- 48. Bar-Haim Y, Morag I, Glickman S. Training anxious children to disengage attention from threat: A randomized controlled trial. J Child Psychol Psychiatry. 2011;52(8):861-9. doi: 10.1111/j.1469-7610.2011.02368.x. PMID: 2011-14641-007. Exclusion Code: X3.
- 49. Barnes AJ. Attachment-based family therapy reduces suicidal ideation in adolescents. Evid

- Based Ment Health. 2011 Feb;14(1):8. doi: 10.1136/ebmh.14.1.8. PMID: 21266605. Exclusion Code: X8.
- 50. Barrett PM. Evaluation of cognitive-behavioral group treatments for childhood anxiety disorders. J Clin Child Psychol. 1998 Dec;27(4):459-68. doi: 10.1207/s15374424jccp2704_10. PMID: 9866083. Exclusion Code: X13.
- 51. Beidel DC, Turner SM, Morris TL. Behavioral treatment of childhood social phobia. J Consult Clin Psychol. 2000 Dec;68(6):1072-80. PMID: 11142541. Exclusion Code: X4.
- Beidel DC, Turner SM, Sallee FR, et al. SET-C versus fluoxetine in the treatment of childhood social phobia. J Am Acad Child Adolesc Psychiatry. 2007;46(12):1622-32. doi: 10.1097/chi.0b013e318154bb57. PMID: 2007-18374-011. Exclusion Code: X13.
- 53. Beitchman JH, Kruidenier B, Clegg M. The Children's Self-Report Rating Scale: screening accuracy and predictive power reconsidered. J Am Acad Child Adolesc Psychiatry. 1987 Jan;26(1):49-52. doi: 10.1097/00004583-198701000-00010. PMID: 3584000. Exclusion Code: X2.
- 54. Berard R, Fong R, Carpenter DJ, et al. An international, multicenter, placebo-controlled trial of paroxetine in adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2006 Feb-Apr;16(1-2):59-75. doi: 10.1089/cap.2006.16.59. PMID: 16553529. Exclusion Code: X3.
- 55. Berard RMF, Ahmed N. Hospital Anxiety and Depression Scale (HADS) as a screening instrument in a depressed adolescent and young adult population. Int J Adolesc Med Health. 1995;8(3):157-66. PMID: 1996-04775-001. Exclusion Code: X2.
- 56. Berg M, Rozental A, de Brun Mangs J, et al. The role of learning support and chat-sessions in guided internet-based cognitive behavioral therapy for adolescents with anxiety: a factorial design study. Front Psychiatry. 2020;11:503. doi: 10.3389/fpsyt.2020.00503. PMID: 32587533. Exclusion Code: X4.
- 57. Berg M, Rozental A, Johansson S, et al. The role of knowledge in internet-based cognitive behavioural therapy for adolescent depression: Results from a randomised controlled study. Internet Interv. 2019 Mar;15:10-7. doi: 10.1016/j.invent.2018.10.001. PMID: 30519531. Exclusion Code: X9.
- 58. Berge KG, Agdal ML, Vika M, et al. Treatment of intra-oral injection phobia: a randomized delayed intervention controlled trial among Norwegian 10- to 16-year-olds. Acta Odontol Scand. 2017 May;75(4):294-301. doi: 10.1080/00016357.2017.1297849. PMID: 28270029. Exclusion Code: X2.
- Bergeron L, Smolla N, Berthiaume C, et al. Reliability, validity, and clinical utility of the Dominic Interactive for Adolescents-revised (a

- DSM-5-based self-report screen for mental disorders, borderline personality traits, and suicidality). Can J Psychiatry. 2017 Mar;62(3):211-22. doi: 10.1177/0706743716670129. PMID: 27638424. Exclusion Code: X3.
- 60. Bernard DL, Calhoun CD, Banks DE, et al.
 Making the "C-ACE" for a Culturally-informed
 Adverse Childhood experiences framework to
 understand the pervasive mental health impact of
 racism on Black youth. J Child Adolesc Trauma.
 2021 Jun;14(2):233-47. doi: 10.1007/s40653020-00319-9. PMID: 33986909. Exclusion Code:
 X7
- 61. Bernstein GA, Anderson LK, Hektner JM, et al. Imipramine compliance in adolescents. J Am Acad Child Adolesc Psychiatry. 2000 Mar;39(3):284-91. doi: 10.1097/00004583-200003000-00009. PMID: 10714047. Exclusion Code: X3.
- 62. Bernstein GA, Borchardt CM, Perwien AR, et al. Imipramine plus cognitive-behavioral therapy in the treatment of school refusal. J Am Acad Child Adolesc Psychiatry. 2000 Mar;39(3):276-83. doi: 10.1097/00004583-200003000-00008. PMID: 10714046. Exclusion Code: X3.
- 63. Bhatta S, Champion JD, Young C, et al.
 Outcomes of depression screening among
 adolescents accessing school-based pediatric
 primary care clinic services. J Pediatr Nurs. 2018
 Jan-Feb;38:8-14. doi:
 10.1016/j.pedn.2017.10.001. PMID: 29167086.
 Exclusion Code: X3.
- Biederman J. Clonazepam in the treatment of prepubertal children with panic-like symptoms. J
 Clin Psychiatry. 1987 Oct;48 Suppl:38-42.
 PMID: 3667548. Exclusion Code: X3.
- 65. Bierman KL, Heinrichs BS, Welsh JA, et al. Reducing adolescent psychopathology in socioeconomically disadvantaged children with a preschool intervention: a randomized controlled trial. The American Journal of Psychiatry. 2020 December 10, 2020;178(4):305-12. doi: 10.1176/appi.ajp.2020.20030343. Exclusion Code: X2.
- 66. Bilek EL, Ehrenreich-May J. An open trial investigation of a transdiagnostic group treatment for children with anxiety and depressive symptoms. Behav Ther. 2012;43(4):887-97. doi: 10.1016/j.beth.2012.04.007. PMID: 2012-27520-008. Exclusion Code: X7.
- 67. Birmaher B, Waterman GS, Ryan N, et al. Fluoxetine for childhood anxiety disorders. J Am Acad Child Adolesc Psychiatry. 1994 Sep;33(7):993-9. doi: 10.1097/00004583-199409000-00009. PMID: 7961355. Exclusion Code: X2.
- 68. Blom EH, Larsson JO, Serlachius E, et al. The differentiation between depressive and anxious adolescent females and controls by behavioural self-rating scales. J Affect Disord. 2010 May;122(3):232-40. doi:

- 10.1016/j.jad.2009.07.006. PMID: 19695710. Exclusion Code: X7.
- 69. Blossom JB, Ginsburg GS, Birmaher B, et al. Parental and family factors as predictors of threat bias in anxious youth. Cognit Ther Res. 2013;37(4):812-9. doi: 10.1007/s10608-012-9513-0. PMID: 2013-00135-001. Exclusion Code: X7.
- 70. Bodden DH, Bögels SM, Muris P. The diagnostic utility of the Screen for Child Anxiety Related Emotional Disorders-71 (SCARED-71). Behav Res Ther. 2009 May;47(5):418-25. doi: 10.1016/j.brat.2009.01.015. PMID: 19230863. Exclusion Code: X4.
- 71. Bodden DH, Dirksen CD, Bögels SM, et al. Costs and cost-effectiveness of family CBT versus individual CBT in clinically anxious children. Clin Child Psychol Psychiatry. 2008 Oct;13(4):543-64. doi: 10.1177/1359104508090602. PMID: 18927140. Exclusion Code: X4.
- 72. Bottelier MA, Schrantee AGM, Van Wingen GA, et al. Treatment with fluoxetine in adolescents may aggravate emotional dysregulation: a power analysis for future studies. European neuropsychopharmacology. 2015;25:S461-S2. PMID: CN-01163210. Exclusion Code: X9.
- 73. Boudreaux ED, Camargo CA, Jr., Arias SA, et al. Improving suicide risk screening and detection in the emergency department. Am J Prev Med. 2016 Apr;50(4):445-53. doi: 10.1016/j.amepre.2015.09.029. PMID: 26654691. Exclusion Code: X2.
- 74. Boylan C, Morgan S, Carthy A, et al. A randomised controlled trial of a programme for parents and full-time carers of young people with self-harm or suicidal behaviour. Eur Child Adolesc Psychiatry. 2013;22(2):S184-. doi: 10.1007/s00787-013-0423-9. PMID: CN-01006221. Exclusion Code: X2.
- 75. Boyle MH, Cunningham CE, Georgiades K, et al. The Brief Child and Family Phone Interview (BCFPI): 2. Usefulness in screening for child and adolescent psychopatholog. J Child Psychol Psychiatry. 2009 Apr;50(4):424-31. doi: 10.1111/j.1469-7610.2008.01971.x. PMID: 19175807. Exclusion Code: X5.
- 76. Bredemeier K, Spielberg JM, Silton RL, et al. Screening for depressive disorders using the Mood and Anxiety Symptoms Questionnaire Anhedonic Depression Scale: a receiver-operating characteristic analysis. Psychol Assess. 2010 Sep;22(3):702-10. doi: 10.1037/a0019915. PMID: 20822283. Exclusion Code: X2.
- 77. Brent D, Emslie G, Clarke G, et al. Switching to another SSRI or to venlafaxine with or without cognitive behavioral therapy for adolescents with SSRI-resistant depression: the TORDIA randomized controlled trial. JAMA. 2008 Feb 27;299(8):901-13. doi: 10.1001/jama.299.8.901. PMID: 18314433. Exclusion Code: X2.

- 78. Brent DA, Brunwasser SM, Hollon SD, et al. Effect of a cognitive-behavioral prevention program on depression 6 years after implementation among at-risk adolescents: a randomized clinical trial. JAMA Psychiatry. 2015 Nov;72(11):1110-8. doi: 10.1001/jamapsychiatry.2015.1559. PMID: 26421861. Exclusion Code: X2.
- 79. Brent DA, Emslie GJ, Clarke GN, et al.
 Predictors of spontaneous and systematically assessed suicidal adverse events in the treatment of SSRI-resistant depression in adolescents (TORDIA) study. Am J Psychiatry. 2009
 Apr;166(4):418-26. doi:
 10.1176/appi.ajp.2008.08070976. PMID:
 19223438. Exclusion Code: X2.
- 80. Brent DA, Holder D, Kolko D, et al. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. Arch Gen Psychiatry. 1997
 Sep;54(9):877-85. PMID: 9294380. Exclusion Code: X13.
- 81. Brent DA, Kennard BD. Impact of a brief inpatient intervention and suicide safety planning app to decrease suicidal behavior after hospital discharge. J Am Acad Child Adolesc Psychiatry. 2018;57(10):S33-. doi: 10.1016/j.jaac.2018.07.142. PMID: CN-01654953. Exclusion Code: X12.
- 82. Brent DA, Kolko DJ, Birmaher B, et al. Predictors of treatment efficacy in a clinical trial of three psychosocial treatments for adolescent depression. J Am Acad Child Adolesc Psychiatry. 1998 Sep;37(9):906-14. doi: 10.1097/00004583-199809000-00010. PMID: 9735610. Exclusion Code: X4.
- 83. Britton JC, Bar-Haim Y, Clementi MA, et al. Training-associated changes and stability of attention bias in youth: Implications for Attention Bias Modification Treatment for pediatric anxiety. Dev Cogn Neurosci. 2013;4:52-64. doi: 10.1016/j.dcn.2012.11.001. PMID: 2013-09450-006. Exclusion Code: X4.
- 84. Brunoni AR, Sampaio-Junior B, Moffa AH, et al. The Escitalopram versus Electric Current Therapy for Treating Depression Clinical Study (ELECT-TDCS): rationale and study design of a non-inferiority, triple-arm, placebo-controlled clinical trial. Sao Paulo Med J. 2015 May-Jun;133(3):252-63. doi: 10.1590/1516-3180.2014.00351712. PMID: 26176930. Exclusion Code: X2.
- 85. Brunshaw JM, Szatmari P. The agreement between behaviour checklists and structured psychiatric interviews for children. Can J Psychiatry. 1988 Aug;33(6):474-81. doi: 10.1177/070674378803300608. PMID: 3196999. Exclusion Code: X2.
- 86. Bunnell BE, Mesa F, Beidel DC. A two-session hierarchy for shaping successive approximations of speech in selective mutism: pilot study of mobile apps and mechanisms of behavior change.

- Behav Ther. 2018 Nov;49(6):966-80. doi: 10.1016/j.beth.2018.02.003. PMID: 30316494. Exclusion Code: X3.
- 87. Burke TA, Jacobucci R, Ammerman BA, et al. Using machine learning to classify suicide attempt history among youth in medical care settings. J Affect Disord. 2020 May 1;268:206-14. doi: 10.1016/j.jad.2020.02.048. PMID: 32174479. Exclusion Code: X3.
- 88. Busby DR, King CA, Brent D, et al. Adolescents' engagement with crisis hotline risk-management services: a report from the Emergency Department Screen for Teen Suicide Risk (ED-STARS) Study. Suicide Life Threat Behav. 2020 Feb;50(1):72-82. doi: 10.1111/sltb.12558. PMID: 31152463. Exclusion Code: X9.
- 89. Bushnell GA, Stürmer T, Swanson SA, et al. Dosing of Selective Serotonin Reuptake Inhibitors among children and adults before and after the FDA black-box warning. Psychiatr Serv. 2016 Mar;67(3):302-9. doi: 10.1176/appi.ps.201500088. PMID: 26567938. Exclusion Code: X3.
- Canals J DE, Carbajo G, Blade J. Prevalence of DSM-III-R and ICD-10 psychiatric disorders in a Spanish population of 18-year-olds. Acta Psychiatr Scand. 1997;96:287-94. Exclusion Code: X3.
- 91. Canals J M-HC, Fernandez-Ballart J, Domenech E. A longitudinal study of depression in an urban Spanish pubertal population. Eur Child Adolesc Psychiatry. 1995;4:102-11. Exclusion Code: X9.
- 92. Caporino N. Child/adolescent anxiety multimodal extended long-term study: depression and suicide outcomes. J Am Acad Child Adolesc Psychiatry. 2017;56(10):S318-. doi: 10.1016/j.jaac.2017.07.639. PMID: CN-01452306. Exclusion Code: X9.
- 93. Caporino NE, Brodman DM, Kendall PC, et al. Defining treatment response and remission in child anxiety: signal detection analysis using the pediatric anxiety rating scale. J Am Acad Child Adolesc Psychiatry. 2013 Jan;52(1):57-67. doi: 10.1016/j.jaac.2012.10.006. PMID: 23265634. Exclusion Code: X10.
- 94. Caporino NE, Sakolsky D, Brodman DM, et al. Establishing clinical cutoffs for response and remission on the Screen for Child Anxiety Related Emotional Disorders (SCARED). J Am Acad Child Adolesc Psychiatry. 2017 Aug;56(8):696-702. doi: 10.1016/j.jaac.2017.05.018. PMID: 28735699. Exclusion Code: X3.
- 95. Caron EB, Drake KL, Stewart CE, et al.
 Intervention adherence and self-efficacy as
 predictors of child outcomes in school nursedelivered interventions for anxiety. J Sch Nurs.
 2020 May 15:1059840520925522. doi:
 10.1177/1059840520925522. PMID: 32410495.
 Exclusion Code: X4.
- 96. Cartwright-Hatton S, McNally D, Field AP, et al. A new parenting-based group intervention for

- young anxious children: Results of a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2011;50(3):242-51. doi: 10.1016/j.jaac.2010.12.015. PMID: 2011-04926-006. Exclusion Code: X3.
- 97. Cederlund R, Öst L-G. Psychometric properties of the Social Phobia and Anxiety Inventory-Child version in a Swedish clinical sample. J Anxiety Disord. 2013;27(5):503-11. doi: 10.1016/j.janxdis.2013.06.004. PMID: 2013-31517-009. Exclusion Code: X2.
- 98. Cervin M, Storch EA, Piacentini J, et al.
 Symptom-specific effects of cognitive-behavioral therapy, sertraline, and their combination in a large randomized controlled trial of pediatric anxiety disorders. J Child Psychol Psychiatry.
 2020 Apr;61(4):492-502. doi:
 10.1111/jcpp.13124. PMID: 31471911.
 Exclusion Code: X7.
- 99. Cervin M, Storch EA, Piacentini J, et al.
 Symptom-specific effects of cognitive-behavioral therapy, sertraline, and their combination in a large randomized controlled trial of pediatric anxiety disorders. Journal of child psychology & psychiatry. 2020;61(4):492-502. doi: 10.1111/jcpp.13124. PMID: CN-02127722. Exclusion Code:
- 100. Chanen AM, Jackson HJ, McCutcheon LK, et al. Early intervention for adolescents with borderline personality disorder using cognitive analytic therapy: randomised controlled trial. Br J Psychiatry. 2008 Dec;193(6):477-84. doi: 10.1192/bjp.bp.107.048934. PMID: 19043151. Exclusion Code: X4.
- 101. Chang SW, Kuckertz JM, Bose D, et al. Efficacy of attention bias training for child anxiety disorders: a randomized controlled trial. Child Psychiatry Hum Dev. 2019 Apr;50(2):198-208. doi: 10.1007/s10578-018-0832-6. PMID: 30051155. Exclusion Code: X3.
- 102. Chapdelaine A, Carrier JD, Fournier L, et al.
 Treatment adequacy for social anxiety disorder in
 primary care patients. PLoS One.
 2018;13(11):e0206357. doi:
 10.1371/journal.pone.0206357. PMID:
 30395608. Exclusion Code: X2.
- 103. Charkhandeh M, Talib MA, Hunt CJ. The clinical effectiveness of cognitive behavior therapy and an alternative medicine approach in reducing symptoms of depression in adolescents. Psychiatry Res. 2016 May 30;239:325-30. doi: 10.1016/j.psychres.2016.03.044. PMID: 27058159. Exclusion Code: X6.
- 104. Chavira DA, Stein MB. Combined psychoeducation and treatment with selective serotonin reuptake inhibitors for youth with generalized social anxiety disorder. J Child Adolesc Psychopharmacol. 2002
 Spring;12(1):47-54. doi:
 10.1089/10445460252943560. PMID: 12014595. Exclusion Code: X3.

- 105. Chavira DA, Stein MB, Bailey K, et al. Child anxiety in primary care: prevalent but untreated. Depress Anxiety. 2004;20(4):155-64. doi: 10.1002/da.20039. PMID: 15643639. Exclusion Code: X9
- 106. Chen H, Upadhyay N, Lyu N, et al. Association of primary and behavioral health integrated care upon pediatric mental disorder treatment. Acad Pediatr. 2021 Jun 1doi: 10.1016/j.acap.2021.05.021. PMID: 34087480. Exclusion Code: X7.
- 107. Chen S. An online solution focused brief therapy for adolescent anxiety during the novel coronavirus disease (COVID-19) pandemic: a structured summary of a study protocol for a randomised controlled trial. Trials.
 2020;21(1)doi: 10.1186/s13063-020-04355-6.
 PMID: CN-02120850. Exclusion Code: X2.
- 108. Chiappini EA, Gosch E, Compton SN, et al. Insession involvement in anxious youth receiving CBT with/without medication. J Psychopathol Behav Assess. 2020;42(4):615-26. doi: 10.1007/s10862-020-09810-x. PMID: 2020-39041-001. Exclusion Code: X9.
- 109. Chorpita BF, Moffitt CE, Gray J. Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. Behav Res Ther. 2005 Mar;43(3):309-22. doi: 10.1016/j.brat.2004.02.004. PMID: 15680928. Exclusion Code: X5.
- 110. Chowdhury T, Champion JD. Outcomes of depression screening for adolescents accessing pediatric primary care-based services. J Pediatr Nurs. 2020 Mar 2;52:25-9. doi: 10.1016/j.pedn.2020.02.036. PMID: 32135479. Exclusion Code: X7.
- 111. Christensen KS, Haugen W, Sirpal MK, et al. Diagnosis of depressed young people--criterion validity of WHO-5 and HSCL-6 in Denmark and Norway. Fam Pract. 2015 Jun;32(3):359-63. doi: 10.1093/fampra/cmv011. PMID: 25800246. Exclusion Code: X8.
- 112. Chu BC, Carpenter AL, Wyszynski CM, et al. Scalable options for extended skill building following Didactic training in Cognitive-Behavioral Therapy for anxious youth: A Pilot Randomized Trial. J Clin Child Adolesc Psychol. 2017 May-Jun;46(3):401-10. doi: 10.1080/15374416.2015.1038825. PMID: 25984590. Exclusion Code: X2.
- 113. Chu BC, Crocco ST, Esseling P, et al.
 Transdiagnostic group behavioral activation and exposure therapy for youth anxiety and depression: Initial randomized controlled trial.
 Behav Res Ther. 2016 Jan;76:65-75. doi: 10.1016/j.brat.2015.11.005. PMID: 26655958.
 Exclusion Code: X5.
- 114. Chutko L, Surushkina SY, Nikishena I, et al.
 Treatment of anxiety disorders in school
 maladaptation with adaptol. Neurosci Behav
 Physiol. 2011;41(5):520-4. Exclusion Code: X3.

- 115. Cianchetti C, Faedda N, Pasculli M, et al. Predictive validity for the clinical diagnosis of a new parent questionnaire, the CABI, compared with CBCL. Clin Child Psychol Psychiatry. 2020 Apr;25(2):507-19. doi: 10.1177/1359104519895056. PMID: 31894698. Exclusion Code: X2.
- 116. Clarke G, Sheppler CR, Firemark AJ, et al. Augmenting usual care SSRIs with cognitive behavioral therapy for insomnia to improve depression outcomes in youth: Design of a randomized controlled efficacy-effectiveness trial. Contemp Clin Trials. 2020 Feb 28;91:105967. doi: 10.1016/j.cct.2020.105967. PMID: 32114185. Exclusion Code: X4.
- 117. Clarke GN, Hornbrook M, Lynch F, et al. Group cognitive-behavioral treatment for depressed adolescent offspring of depressed parents in a health maintenance organization. J Am Acad Child Adolesc Psychiatry. 2002 Mar;41(3):305-13. doi: 10.1097/00004583-200203000-00010. PMID: 11886025. Exclusion Code: X2.
- 118. Clément C, Lin J, Stangier U. Efficacy of behavioral experiments in Cognitive Therapy for social anxiety disorder: study protocol for a randomized controlled trial. Trials. 2019 Dec 19;20(1):748. doi: 10.1186/s13063-019-3905-3. PMID: 31856903. Exclusion Code: X4.
- Cobham VE. Do anxiety-disordered children need to come into the clinic for efficacious treatment? J Consult Clin Psychol.
 2012;80(3):465-76. doi: 10.1037/a0028205.
 PMID: 2012-10793-001. Exclusion Code: X13.
- 120. Cobham VE, Dadds MR, Spence SH. The role of parental anxiety in the treatment of childhood anxiety. J Consult Clin Psychol. 1998

 Dec;66(6):893-905. doi: 10.1037//0022-006x.66.6.893. PMID: 9874902. Exclusion Code: X3.
- 121. Cohen JR, So FK, Young JF, et al. Youth depression screening with parent and self-reports: assessing current and prospective depression risk. Child Psychiatry Hum Dev. 2019 Aug;50(4):647-60. doi: 10.1007/s10578-019-00869-6. PMID: 30737605. Exclusion Code: X7.
- 122. Coker TR, Porras-Javier L, Zhang L, et al. 4.57 Improved Access to Mental Health Care Using a Telehealth-Enhanced Referral Process in Pediatric Primary Care: a Cluster Randomized Trial. J Am Acad Child Adolesc Psychiatry. 2018;57(10):S222-. doi: 10.1016/j.jaac.2018.09.282. PMID: CN-01653032. Exclusion Code: X2.
- 123. Colins O, Grisso T, Vahl P, et al. Standardized screening for mental health needs of detained youths from various ethnic origins: the Dutch Massachusetts Youth Screening Instrument-Second Version (MAYSI-2). Journal of Psychopathology & Behavioral Assessment. 2015;37(3):481-92. doi: 10.1007/s10862-014-9476-4. PMID: 109827440. Language: English. Entry Date: 20150812. Revision Date: 20160831.

- Publication Type: Journal Article. Exclusion Code: X9.
- 124. Comer JS, Furr JM, del Busto C, et al. Therapistled, internet-delivered treatment for early child social anxiety: a waitlist-controlled evaluation of the iCALM Telehealth Program. Behav Ther. 2021doi: 10.1016/j.beth.2021.01.004. PMID: CN-02276119. Exclusion Code: X3.
- 125. Compton SN, Grant PJ, Chrisman AK, et al.
 Sertraline in children and adolescents with social
 anxiety disorder: an open trial. J Am Acad Child
 Adolesc Psychiatry. 2001 May;40(5):564-71. doi:
 10.1097/00004583-200105000-00016. PMID:
 11349701. Exclusion Code: X4.
- 126. Conner OL, Siegle GJ, McFarland AM, et al. Mom—It helps when you're right here!

 Attenuation of neural stress markers in anxious youths whose caregivers are present during fMRI. PLoS One. 2012;7(12)doi: 10.1371/journal.pone.0050680. PMID: 2013-12066-001. Exclusion Code: X3.
- 127. Conway PM, Erlangsen A, Teasdale TW, et al. Predictive validity of the Columbia-Suicide Severity Rating Scale for short-term suicidal behavior: a Danish study of adolescents at a high risk of suicide. Arch Suicide Res. 2017 Jul 3;21(3):455-69. doi: 10.1080/13811118.2016.1222318. PMID: 27602917. Exclusion Code: X2.
- 128. Cooper WO, Callahan ST, Shintani A, et al.
 Antidepressants and suicide attempts in children.
 Pediatrics. 2014 Feb;133(2):204-10. doi:
 10.1542/peds.2013-0923. PMID: 24394688.
 Exclusion Code: X4.
- 129. Cornwall E, Spence SH, Schotte D. The effectiveness of emotive imagery in the treatment of darkness phobia in children. Behav Change. 1996;13(4):223-9. Exclusion Code: X3.
- 130. Cortez AB, Wilkins J, Handler E, et al. Multistage adolescent depression screening: a comparison of 11-year-olds to 12-year-olds. Perm J. 2021 May;25doi: 10.7812/tpp/20.233. PMID: 33970080. Exclusion Code: X7.
- 131. Cosi S, Canals J, Hernández-Martinez C, et al. Parent-child agreement in SCARED and its relationship to anxiety symptoms. J Anxiety Disord. 2010 Jan;24(1):129-33. doi: 10.1016/j.janxdis.2009.09.008. PMID: 19864109. Exclusion Code: X9.
- 132. Costello LH, Suh C, Burnett B, et al. Addressing adolescent depression in primary care: building capacity through psychologist and pediatrician partnership. J Clin Psychol Med Settings. 2019 Nov 20doi: 10.1007/s10880-019-09680-w. PMID: 31749100. Exclusion Code: X4.
- 133. Cotton S, Kraemer KM, Sears RW, et al.

 Mindfulness-based cognitive therapy for children
 and adolescents with anxiety disorders at-risk for
 bipolar disorder: A psychoeducation waitlist
 controlled pilot trial. Early Intervention in
 Psychiatry. 2020;14(2):211-9. doi:

- 10.1111/eip.12848. PMID: 2019-37562-001. Exclusion Code: X7.
- 134. Courtney-Seidler EA, Burns K, Zilber I, et al.
 Adolescent suicide and self-injury: deepening the
 understanding of the biosocial theory and
 applying dialectical behavior therapy.
 International Journal of Behavioral Consultation
 and Therapy. 2014;9(3):35-40. doi:
 10.1037/h0101638. PMID: 2019-11792-008.
 Exclusion Code: X8.
- 135. Crane ME, Norris LA, Frank HE, et al. Impact of treatment improvement on long-term anxiety: results from CAMS and CAMELS. J Consult Clin Psychol. 2021 Feb;89(2):126-33. doi: 10.1037/ccp0000523. PMID: 33705168. Exclusion Code: X9.
- 136. Creswell C, Cruddace S, Gerry S, et al.
 Treatment of childhood anxiety disorder in the context of maternal anxiety disorder: a randomised controlled trial and economic analysis. Health Technol Assess. 2015
 May;19(38):1-184, vii-viii. doi:
 10.3310/hta19380. PMID: 26004142. Exclusion Code: X7.
- 137. Cuijpers P, Smits N, Donker T, et al. Screening for mood and anxiety disorders with the fiveitem, the three-item, and the two-item Mental Health Inventory. Psychiatry Res. 2009 Aug 15;168(3):250-5. doi: 10.1016/j.psychres.2008.05.012. PMID: 19185354. Exclusion Code: X2.
- 138. Cunha M, Gouveia JP, do Céu Salvador M. Social fears in adolescence: the social anxiety and avoidance scale for adolescents. Eur Psychol. 2008;13(3):197-213. doi: 10.1027/1016-9040.13.3.197. PMID: 2008-13222-006. Exclusion Code: X13.
- 139. Cwik M, Jay S, Ryan TC, et al. Lowering the Age Limit in Suicide Risk Screening: Clinical Differences and Screening Form Predictive Ability. J Am Acad Child Adolesc Psychiatry. 2021 May;60(5):537-40. doi: 10.1016/j.jaac.2020.11.025. PMID: 33667604. Exclusion Code: X4.
- 140. da Costa CZ, de Morais RM, Zanetta DM, et al. Comparison among clomipramine, fluoxetine, and placebo for the treatment of anxiety disorders in children and adolescents. J Child Adolesc Psychopharmacol. 2013 Dec;23(10):687-92. doi: 10.1089/cap.2012.0110. PMID: 24350814. Exclusion Code: X6.
- D'Amato G. Chlordiazepoxide in management of school phobia. Dis Nerv Syst. 1962 May;23:292-5. PMID: 13882945. Exclusion Code: X2.
- Dams J, Kronmuller KT, Leibing E, et al. Direct costs of social phobia in adolescents and cost-effectiveness of psychotherapy. Psychiatr Prax. 2019;46(3):148-55. doi: 10.1055/a-0733-4999.
 PMID: CN-01937705. Exclusion Code: X1.
- 143. Dardas LA. Family functioning moderates the impact of depression treatment on adolescents' suicidal ideations. Child & Adolescent Mental

- Health. 2019;24(3):251-8. doi: 10.1111/camh.12323. PMID: 138125078. Language: English. Entry Date: 20190821. Revision Date: 20200122. Publication Type: Article. Exclusion Code: X9.
- 144. de Groot J, Cobham V, Leong J, et al. Individual versus group family-focused cognitive-behaviour therapy for childhood anxiety: pilot randomized controlled trial. Aust N Z J Psychiatry. 2007 Dec;41(12):990-7. doi: 10.1080/00048670701689436. PMID: 17999271. Exclusion Code: X3.
- 145. de Haan A, Petermann F, Meiser-Stedman R, et al. Psychometric properties of the German version of the Child Post-Traumatic Cognitions Inventory (CPTCI-GER). Child Psychiatry Hum Dev. 2016;47(1):151-8. doi: 10.1007/s10578-015-0552-0. PMID: 2015-23379-001. Exclusion Code: X3.
- De Lijster JM, Dieleman GC, Utens E, et al.
 Online Attention Bias Modification in
 Combination with Cognitive-Behavioural
 Therapy for Children and Adolescents with
 Anxiety Disorders: a Randomised Controlled
 Trial. Behav Change. 2019doi:
 10.1017/bec.2019.8. PMID: CN-01937771.
 Exclusion Code: X4.
- 147. de Wilde EJ, van de Looij P, Goldschmeding J, et al. Self-report of suicidal thoughts and behavior vs. school nurse evaluations in Dutch high-school students. Crisis. 2011;32(3):121-7. doi: 10.1027/0227-5910/a000064. PMID: 21616760. Exclusion Code: X9.
- 148. Deas D, Randall CL, Roberts JS, et al. A double-blind, placebo-controlled trial of sertraline in depressed adolescent alcoholics: a pilot study. Hum Psychopharmacol. 2000 Aug;15(6):461-9. doi: 10.1002/1099-1077(200008)15:6<461::aid-hup209>3.0.co;2-j. PMID: 12404308. Exclusion Code: X2.
- DelBello MP, Hochadel TJ, Portland KB, et al. A double-blind, placebo-controlled study of selegiline transdermal system in depressed adolescents. J Child Adolesc Psychopharmacol. 2014 Aug;24(6):311-7. doi: 10.1089/cap.2013.0138. PMID: 24955812. Exclusion Code: X3.
- Desousa DA, Salum GA, Isolan LR, et al. Sensitivity and specificity of the Screen for Child Anxiety Related Emotional Disorders (SCARED): a community-based study. Child Psychiatry Hum Dev. 2013 Jun;44(3):391-9. doi: 10.1007/s10578-012-0333-y. PMID: 22961135. Exclusion Code: X6.
- 151. DeVylder JE, Ryan TC, Cwik M, et al. Screening for suicide risk among youths with a psychotic disorder in a pediatric emergency department.

 Psychiatr Serv. 2020 Feb 1;71(2):205-8. doi: 10.1176/appi.ps.201900290. PMID: 31795855.

 Exclusion Code: X5.
- 152. DeVylder JE, Ryan TC, Cwik M, et al. Assessment of selective and universal screening

- for suicide risk in a pediatric emergency department. JAMA Netw Open. 2019 Oct 2;2(10):e1914070. doi: 10.1001/jamanetworkopen.2019.14070. PMID: 31651971. Exclusion Code: X4.
- 153. Dewis LM, Kirkby KC, Martin F, et al.
 Computer-aided vicarious exposure versus live
 graded exposure for spider phobia in children. J
 Behav Ther Exp Psychiatry. 2001 Mar;32(1):1727. doi: 10.1016/s0005-7916(01)00019-2. PMID:
 11729943. Exclusion Code: X2.
- 154. Di Simplicio M, Appiah-Kusi E, Wilkinson P, et al. Imaginator: a proof-of-concept feasibility trial of a brief imagery-based psychological intervention for young people who self-harm. Suicide Life Threat Behav. 2020 Jun;50(3):724-40. doi: 10.1111/sltb.12620. PMID: 32057131. Exclusion Code: X13.
- 155. Diamond G, Creed T, Gillham J, et al. Sexual trauma history does not moderate treatment outcome in Attachment-Based Family Therapy (ABFT) for adolescents with suicide ideation. J Fam Psychol. 2012 Aug;26(4):595-605. doi: 10.1037/a0028414. PMID: 22709259. Exclusion Code: X2.
- 156. Diamond GM, Diamond GS, Levy S, et al.
 Attachment-based family therapy for suicidal lesbian, gay, and bisexual adolescents: a treatment development study and open trial with preliminary findings. Psychotherapy (chicago, ill.). 2012;49(1):62-71. doi: 10.1037/a0026247. PMID: CN-00900412. Exclusion Code: X4.
- 157. Diamond GS, Reis BF, Diamond GM, et al. Attachment-based family therapy for depressed adolescents: a treatment development study. J Am Acad Child Adolesc Psychiatry. 2002 Oct;41(10):1190-6. doi: 10.1097/00004583-200210000-00008. PMID: 12364840. Exclusion Code: X13.
- 158. Dickerson JF, Lynch FL, De Bar L, et al. Costeffectiveness of a brief primary care cognitive behavioral therapy intervention for depressed adolescents who decline pharmacotherapy. Journal of mental health policy and economics. 2015;18:S9-S10. PMID: CN-01142724. Exclusion Code: X9.
- 159. Dickerson JF, Lynch FL, Leo MC, et al. costeffectiveness of cognitive behavioral therapy for depressed youth declining antidepressants. Pediatrics. 2018 Feb;141(2)doi: 10.1542/peds.2017-1969. PMID: 29351965. Exclusion Code: X9.
- Dietz LJ, Marshal MP, Burton CM, et al. Social problem solving among depressed adolescents is enhanced by structured psychotherapies. J Consult Clin Psychol. 2014 Apr;82(2):202-11. doi: 10.1037/a0035718. PMID: 24491077. Exclusion Code: X4.
- 161. Dietz LJ, Mufson L, Irvine H, et al. Family-based interpersonal psychotherapy for depressed preadolescents: an open-treatment trial. Early Interv Psychiatry. 2008 Aug;2(3):154-61. doi:

- 10.1111/j.1751-7893.2008.00077.x. PMID: 21352148. Exclusion Code: X7.
- Dietz LJ, Weinberg RJ, Brent DA, et al. Family-based interpersonal psychotherapy for depressed preadolescents: examining efficacy and potential treatment mechanisms. J Am Acad Child Adolesc Psychiatry. 2015 Mar;54(3):191-9. doi: 10.1016/j.jaac.2014.12.011. PMID: 25721184. Exclusion Code: X4.
- 163. Do R, Lee S, Kim JS, et al. Effectiveness and dissemination of computer-based cognitive behavioral therapy for depressed adolescents: Effective and accessible to whom? J Affect Disord. 2021 Mar 1;282:885-93. doi: 10.1016/j.jad.2020.12.177. PMID: 33601732. Exclusion Code: X2.
- 164. Dobson ET, Strawn JR. Pharmacotherapy for pediatric generalized anxiety disorder: a systematic evaluation of efficacy, safety and tolerability. Paediatr Drugs. 2016 Feb;18(1):45-53. doi: 10.1007/s40272-015-0153-1. PMID: 26660158. Exclusion Code: X9.
- Donaldson D, Spirito A, Esposito-Smythers C. Treatment for adolescents following a suicide attempt: results of a pilot trial. J Am Acad Child Adolesc Psychiatry. 2005 Feb;44(2):113-20. doi: 10.1097/00004583-200502000-00003. PMID: 15689724. Exclusion Code: X4.
- Donohue MR, Hoyniak CP, Tillman R, et al. Callous-unemotional traits as an intervention target and moderator of parent-child interaction therapy-emotion development treatment for preschool depression and conduct problems. J Am Acad Child Adolesc Psychiatry. 2021 May 20doi: 10.1016/j.jaac.2021.03.018. PMID: 33865929. Exclusion Code: X9.
- 167. Donovan CL, Cobham V, Waters AM, et al. Intensive group-based CBT for child social phobia: a pilot study. Behav Ther. 2015
 May;46(3):350-64. doi:
 10.1016/j.beth.2014.12.005. PMID: 25892171.
 Exclusion Code: X7.
- Donovan CL, Spence SH, March S. Does an online CBT program for anxiety impact upon sleep problems in anxious youth? J Clin Child Adolesc Psychol. 2017 Mar-Apr;46(2):211-21. doi: 10.1080/15374416.2016.1188700. PMID: 27492674. Exclusion Code: X7.
- 169. Downey VA, Zun LS. Identifying Undiagnosed Pediatric Mental Illness in the Emergency Department. Pediatr Emerg Care. 2018 Feb;34(2):e21-e3. doi: 10.1097/pec.000000000001151. PMID: 28441242. Exclusion Code: X7.
- 170. Dummit ES, 3rd, Klein RG, Tancer NK, et al. Fluoxetine treatment of children with selective mutism: an open trial. J Am Acad Child Adolesc Psychiatry. 1996 May;35(5):615-21. doi: 10.1097/00004583-199605000-00016. PMID: 8935208. Exclusion Code: X4.
- 171. Ebesutani C, Bernstein A, Nakamura BJ, et al. A psychometric analysis of the Revised Child

- Anxiety and Depression Scale—Parent Version in a clinical sample. J Abnorm Child Psychol. 2010;38(2):249-60. doi: 10.1007/s10802-009-9363-8. PMID: 2010-02865-009. Exclusion Code: X9.
- 172. Ebesutani C, Korathu-Larson P, Nakamura BJ, et al. The Revised Child Anxiety and Depression Scale 25-Parent version: Scale development and validation in a school-based and clinical sample. Assessment. 2017 Sep;24(6):712-28. doi: 10.1177/1073191115627012. PMID: 26834091. Exclusion Code: X5.
- 173. Ebesutani C, Reise SP, Chorpita BF, et al. The Revised Child Anxiety and Depression Scale-Short version: scale reduction via exploratory bifactor modeling of the broad anxiety factor. Psychol Assess. 2012 Dec;24(4):833-45. doi: 10.1037/a0027283. PMID: 22329531. Exclusion Code: X3.
- 174. Ebesutani C, Tottenham N, Chorpita B. The Revised Child Anxiety and Depression Scale Parent version: extended applicability and validity for use with younger youth and children with histories of early-life caregiver neglect. J Psychopathol Behav Assess. 2015
 Dec;37(4):705-18. doi: 10.1007/s10862-015-9494-x. PMID: 30364688. Exclusion Code: X7.
- 175. Ebrahiminejad S, Poursharifi H, Bakhshiour Roodsari A, et al. The effectiveness of mindfulness-based cognitive therapy on Iranian female adolescents suffering from social anxiety. Iran Red Crescent Med J. 2016
 Nov;18(11):e25116. doi: 10.5812/ircmj.25116.
 PMID: 28191335. Exclusion Code: X5.
- 176. Eggert LL, Thompson EA, Randell BP, et al. Preliminary effects of brief school-based prevention approaches for reducing youth suicide--risk behaviors, depression, and drug involvement. J Child Adolesc Psychiatr Nurs. 2002 Apr-Jun;15(2):48-64. doi: 10.1111/j.1744-6171.2002.tb00326.x. PMID: 12083753. Exclusion Code: X5.
- 177. Elkins RM, Gallo KP, Pincus DB, et al. Moderators of intensive CBT for adolescent panic disorder: the of fear and avoidance. Child Adolesc Ment Health. 2016 Feb 1;21(1):30-6. doi: 10.1111/camh.12122. PMID: 26929742. Exclusion Code: X4.
- 178. Emslie GJ, Heiligenstein JH, Hoog SL, et al. Fluoxetine treatment for prevention of relapse of depression in children and adolescents: a double-blind, placebo-controlled study. J Am Acad Child Adolesc Psychiatry. 2004 Nov;43(11):1397-405. doi: 10.1097/01.chi.0000140453.89323.57. PMID: 15502599. Exclusion Code: X3.
- 179. Emslie GJ, Heiligenstein JH, Wagner KD, et al. Fluoxetine for acute treatment of depression in children and adolescents: a placebo-controlled, randomized clinical trial. J Am Acad Child Adolesc Psychiatry. 2002 Oct;41(10):1205-15. doi: 10.1097/00004583-200210000-00010. PMID: 12364842. Exclusion Code: X13.

- 180. Emslie GJ, Kennard BD, Mayes TL, et al.
 Continued effectiveness of relapse prevention
 cognitive-behavioral therapy following
 Fluoxetine treatment in youth with major
 depressive disorder. J Am Acad Child Adolesc
 Psychiatry. 2015 Dec;54(12):991-8. doi:
 10.1016/j.jaac.2015.09.014. PMID: 26598474.
 Exclusion Code: X7.
- 181. Emslie GJ, Kennard BD, Mayes TL, et al. Fluoxetine versus placebo in preventing relapse of major depression in children and adolescents. Am J Psychiatry. 2008 Apr;165(4):459-67. doi: 10.1176/appi.ajp.2007.07091453. PMID: 18281410. Exclusion Code: X2.
- 182. Emslie GJ, Prakash A, Zhang Q, et al. A doubleblind efficacy and safety study of duloxetine fixed doses in children and adolescents with major depressive disorder. J Child Adolesc Psychopharmacol. 2014 May;24(4):170-9. doi: 10.1089/cap.2013.0096. PMID: 24815533. Exclusion Code: X13.
- 183. Emslie GJ, Rush AJ, Weinberg WA, et al. A double-blind, randomized, placebo-controlled trial of fluoxetine in children and adolescents with depression. Arch Gen Psychiatry. 1997
 Nov;54(11):1031-7. PMID: 9366660. Exclusion Code: X13.
- 184. Emslie GJ, Wagner KD, Kutcher S, et al.
 Paroxetine treatment in children and adolescents
 with major depressive disorder: a randomized,
 multicenter, double-blind, placebo-controlled
 trial. J Am Acad Child Adolesc Psychiatry. 2006
 Jun;45(6):709-19. doi:
 10.1097/01.chi.0000214189.73240.63. PMID:
 16721321. Exclusion Code: X3.
- 185. Enns MW, Cox BJ. Psychosocial and clinical predictors of symptom persistence vs remission in major depressive disorder. Can J Psychiatry. 2005 Oct;50(12):769-77. doi: 10.1177/070674370505001206. PMID: 16408525. Exclusion Code: X3.
- 186. Esbjørn BH, Normann N, Christiansen BM, et al. The efficacy of group metacognitive therapy for children (MCT-c) with generalized anxiety disorder: An open trial. J Anxiety Disord. 2018 Jan;53:16-21. doi: 10.1016/j.janxdis.2017.11.002. PMID: 29145078. Exclusion Code: X4.
- 187. Esposito M, Gimigliano F, Barillari MR, et al. Pediatric selective mutism therapy: a randomized controlled trial. Eur J Phys Rehabil Med. 2017 Oct;53(5):643-50. doi: 10.23736/s1973-9087.16.04037-5. PMID: 27830922. Exclusion Code: X3.
- 188. Esposito-Smythers C, Spirito A, Kahler CW, et al. Treatment of co-occurring substance abuse and suicidality among adolescents: a randomized trial. J Consult Clin Psychol. 2011;79(6):728-39. doi: 10.1037/a0026074. PMID: CN-00837414. Exclusion Code: X2.
- 189. Esposito-Smythers C, Walsh A, Spirito A, et al. Working with the suicidal client who also abuses substances. Cogn Behav Pract. 2012

- May;19(2):245-55. doi: 10.1016/j.cbpra.2010.11.004. PMID: 23209362. Exclusion Code: X2.
- 190. Etter DJ, McCord A, Ouyang F, et al. Suicide screening in primary care: use of an electronic screener to assess suicidality and improve provider follow-up for adolescents. J Adolesc Health. 2018 Feb;62(2):191-7. doi: 10.1016/j.jadohealth.2017.08.026. PMID: 29195764. Exclusion Code: X4.
- 191. Evans L, Haeberlein K, Chang A, et al.
 Convergent Validity and Preliminary Cut-Off
 Scores for the Anxiety and Depression Subscales
 of the DASS-21 in US Adolescents. Child
 Psychiatry Hum Dev. 2021 Aug;52(4):579-85.
 doi: 10.1007/s10578-020-01050-0. PMID:
 32816139. Exclusion Code: X4.
- 192. Evans R, Thirlwall K, Cooper P, et al. Using symptom and interference questionnaires to identify recovery among children with anxiety disorders. Psychol Assess. 2017 Jul;29(7):835-43. doi: 10.1037/pas0000375. PMID: 27845527. Exclusion Code: X2.
- 193. Fairbanks JM, Pine DS, Tancer NK, et al. Open fluoxetine treatment of mixed anxiety disorders in children and adolescents. J Child Adolesc Psychopharmacol. 1997 Spring;7(1):17-29. doi: 10.1089/cap.1997.7.17. PMID: 9192539. Exclusion Code: X4.
- 194. Fallucco EM, Blackmore ER, Bejarano CM, et al. Collaborative care: a pilot study of a Child Psychiatry Outpatient Consultation Model for Primary Care Providers. J Behav Health Serv Res. 2017 Jul;44(3):386-98. doi: 10.1007/s11414-016-9513-z. PMID: 27189698. Exclusion Code: X4.
- 195. Farley AM, Gallop RJ, Brooks ES, et al. Identification and management of adolescent depression in a large pediatric care network. J Dev Behav Pediatr. 2020 Feb/Mar;41(2):85-94. doi: 10.1097/dbp.0000000000000750. PMID: 31651619. Exclusion Code: X9.
- 196. Feldhaus CG, Jacobs RH, Watkins ER, et al. Rumination-focused cognitive behavioral therapy decreases anxiety and increases behavioral activation among remitted adolescents. J Child Fam Stud. 2020;29(7):1982-91. doi: 10.1007/s10826-020-01711-7. PMID: 33737799. Exclusion Code: X2.
- 197. Ferdinand RF. Validity of the CBCL/YSR DSM-IV scales anxiety problems and affective problems. J Anxiety Disord. 2008;22(1):126-34. doi: 10.1016/j.janxdis.2007.01.008. PMID: 17321103. Exclusion Code: X2.
- 198. Fernandez Castelao C, Naber K, Altstädt S, et al.
 Two dimensions of social anxiety disorder: A
 pilot study of the Questionnaire for Social
 Anxiety and Social Competence Deficits for
 Adolescents. Child Adolesc Psychiatry Ment
 Health. 2015;9PMID: 2015-46792-001.
 Exclusion Code: X7.

- 199. Fernández-Martínez I, Morales A, Méndez FX, et al. Spanish Adaptation and Psychometric Properties of the Parent Version of the Short Mood and Feelings Questionnaire (SMFQ-P) in a Non-Clinical Sample of Young School-Aged Children. Span J Psychol. 2020 Nov 5;23:e45. doi: 10.1017/sjp.2020.47. PMID: 33148355. Exclusion Code: X9.
- 200. Findling RL, Pagano ME, McNamara NK, et al. The short-term safety and efficacy of fluoxetine in depressed adolescents with alcohol and cannabis use disorders: a pilot randomized placebo-controlled trial. Child Adolesc Psychiatry Ment Health. 2009 Mar 19;3(1):11. doi: 10.1186/1753-2000-3-11. PMID: 19298659. Exclusion Code: X2.
- 201. Fischer G, Brunner R, Parzer P, et al. Short-term psychotherapeutic treatment in adolescents engaging in non-suicidal self-injury: a randomized controlled trial. Trials. 2013 Sep 13;14:294. doi: 10.1186/1745-6215-14-294. PMID: 24034810. Exclusion Code: X11.
- 202. Fitzgerald A, Rawdon C, Dooley B. A randomized controlled trial of attention bias modification training for socially anxious adolescents. Behav Res Ther. 2016 Sep;84:1-8. doi: 10.1016/j.brat.2016.06.003. PMID: 27379745. Exclusion Code: X5.
- 203. Flamarique I, Santosh P, Zuddas A, et al. Development and psychometric properties of the Suicidality: Treatment Occurring in Paediatrics (STOP) Suicidality Assessment Scale (STOP-SAS) in children and adolescents. BMC Pediatr. 2016 Dec 13;16(1):213. doi: 10.1186/s12887-016-0751-2. PMID: 27964729. Exclusion Code: X5.
- 204. Flannery-Schroeder E, Choudhury MS, Kendall PC. Group and individual cognitive-behavioral treatments for youth with anxiety disorders: 1-year follow-up. Cognit Ther Res. 2005;29(2):253-9. doi: 10.1007/s10608-005-3168-z. PMID: 2005-04909-009. Exclusion Code: X4.
- 205. Flannery-Schroeder EC, Kendall PC. Group and individual cognitive-behavioral treatments for youth with anxiety disorders: A randomized clinical trial. Cognit Ther Res. 2000;24(3):251-78. Exclusion Code: X13.
- 206. Flatt N, King N. Brief psycho-social interventions in the treatment of specific childhood phobias: A controlled trial and a 1-year follow-up. Behav Change. 2010;27(3):130-53. doi: 10.1375/bech.27.3.130. PMID: 2010-21638-002. Exclusion Code: X2.
- 207. Forest Laboratories. A randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of citalopram in children and adolescents with depression. Forest Laboratories Clinical Study Register. 2001(1)PMID: CN-00763823. Exclusion Code: X3.
- 208. Friedman RA. Antidepressants' black-box warning--10 years later. N Engl J Med. 2014 Oct

- 30;371(18):1666-8. doi: 10.1056/NEJMp1408480. PMID: 25354101. Exclusion Code: X3.
- 209. Fristad MA, Vesco AT, Young AS, et al. Pilot randomized controlled trial of omega-3 and individual–family psychoeducational psychotherapy for children and adolescents with depression. J Clin Child Adolesc Psychol. 2019;48(Suppl 1):S105-S18. doi: 10.1080/15374416.2016.1233500. PMID: 2019-14393-010. Exclusion Code: X10.
- 210. Fuentes-Rodriguez G, Saez-Castillo AJ, Garcia-Lopez LJ. Psychometric properties of the social anxiety subscale of the Youth Anxiety Measure for DSM-5 (YAM-5-I-SAD) in a clinical sample of Spanish-speaking adolescents. J Affect Disord. 2018 Aug 1;235:68-71. doi: 10.1016/j.jad.2018.02.035. PMID: 29655076. Exclusion Code: X2.
- 211. Fujii C, Renno P, McLeod BD, et al. Intensive cognitive behavioral therapy for anxiety disorders in school-aged children with autism: A preliminary comparison with treatment-as-usual. School Mental Health. 2013;5(1):25-37. Exclusion Code: X2.
- 212. Gale CK, Millichamp J. Generalised anxiety disorder in children and adolescents. BMJ Clin Evid. 2016 Jan 13;2016PMID: 26763675. Exclusion Code: X7.
- 213. Gallagher HM, Rabian BA, McCloskey MS. A brief group cognitive-behavioral intervention for social phobia in childhood. J Anxiety Disord. 2004;18(4):459-79. doi: 10.1016/S0887-6185(03)00027-6. PMID: 2004-14970-002. Exclusion Code: X13.
- 214. Gallo KP, Chan PT, Buzzella BA, et al. The impact of an 8-day intensive treatment for adolescent panic disorder and agoraphobia on comorbid diagnoses. Behav Ther. 2012 Mar;43(1):153-9. doi: 10.1016/j.beth.2011.05.002. PMID: 22304887. Exclusion Code: X13.
- 215. Garcia-Lopez L, Moore HT. Validation and Diagnostic Efficiency of the Mini-SPIN in Spanish-Speaking Adolescents. PLoS One. 2015;10(8):e0135862. doi: 10.1371/journal.pone.0135862. PMID: 26317695. Exclusion Code: X5.
- 216. Garcia-Lopez LJ, Díaz-Castela Mdel M, Muela-Martinez JA, et al. Can parent training for parents with high levels of expressed emotion have a positive effect on their child's social anxiety improvement? J Anxiety Disord. 2014 Dec;28(8):812-22. doi: 10.1016/j.janxdis.2014.09.001. PMID: 25265549. Exclusion Code: X3.
- 217. Gardner W, Lucas A, Kolko DJ, et al. Comparison of the PSC-17 and alternative mental health screens in an at-risk primary care sample. J Am Acad Child Adolesc Psychiatry. 2007 May;46(5):611-8. doi:

- 10.1097/chi.0b013e318032384b. PMID: 17450052. Exclusion Code: X13.
- 218. Garoff FF, Heinonen K, Pesonen A-K, et al.
 Depressed youth: treatment outcome and changes
 in family functioning in individual and family
 therapy. J Fam Ther. 2012 Feb;34(1):4-23. doi:
 10.1111/j.1467-6427.2011.00541.x. PMID:
 104634633. Language: English. Entry Date:
 20120227. Revision Date: 20150711. Publication
 Type: Journal Article. Exclusion Code: X4.
- 219. Garrison CZ JK, Marsteller F, McKeown R, Addy C. A longitudinal study of depressive symptomatology in young adolescents. Am Acad Child Adolesc Psychiatry. 1990;29:581-5. Exclusion Code: X9.
- 220. Geller B, Cooper TB, Graham DL, et al. Pharmacokinetically designed double-blind placebo-controlled study of nortriptyline in 6- to 12-year-olds with major depressive disorder. J Am Acad Child Adolesc Psychiatry. 1992 Jan;31(1):34-44. doi: 10.1097/00004583-199201000-00007. PMID: 1537779. Exclusion Code: X3.
- 221. Geller B, Cooper TB, McCombs HG, et al. Double-blind, placebo-controlled study of nortriptyline in depressed children using a "fixed plasma level" design. Psychopharmacol Bull. 1989;25(1):101-8. PMID: 2672066. Exclusion Code: X3.
- 222. Gibbons RD, Brown CH, Hur K, et al. Suicidal thoughts and behavior with antidepressant treatment: reanalysis of the randomized placebo-controlled studies of fluoxetine and venlafaxine. Arch Gen Psychiatry. 2012 Jun;69(6):580-7. doi: 10.1001/archgenpsychiatry.2011.2048. PMID: 22309973. Exclusion Code: X3.
- 223. Gibbons RD, Kupfer DJ, Frank E, et al. Computerized adaptive tests for rapid and accurate assessment of psychopathology dimensions in youth. J Am Acad Child Adolesc Psychiatry. 2019 Aug 26doi: 10.1016/j.jaac.2019.08.009. PMID: 31465832. Exclusion Code: X2.
- 224. Gil-Bernal F, Hernández-Guzmán L. Cognitivebehavioural treatment in Mexican children with social phobia. Anuario de Psicología/The UB Journal of Psychology. 2009;40(1):89-104. Exclusion Code: X1.
- 225. Ginsburg GS, Becker KD, Drazdowski TK, et al. Treating anxiety disorders in inner city schools: Results from a pilot randomized controlled trial comparing CBT and usual care. Child & Youth Care Forum. 2012;41(1):1-19. doi: 10.1007/s10566-011-9156-4. PMID: 2012-02360-001. Exclusion Code: X4.
- 226. Ginsburg GS, Becker-Haimes EM, Keeton C, et al. Results from the Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS): primary anxiety outcomes. J Am Acad Child Adolesc Psychiatry. 2018 Jul;57(7):471-80. doi:

- 10.1016/j.jaac.2018.03.017. PMID: 29960692. Exclusion Code: X4.
- 227. Ginsburg GS, Drake KL. School-based treatment for anxious african-american adolescents: a controlled pilot study. J Am Acad Child Adolesc Psychiatry. 2002 Jul;41(7):768-75. doi: 10.1097/00004583-200207000-00007. PMID: 12108800. Exclusion Code: X5.
- 228. Ginsburg GS, Keeton CP, Drazdowski TK, et al. The utility of clinicians ratings of anxiety using the Pediatric Anxiety Rating Scale (PARS). Child & Youth Care Forum. 2011;40(2):93-105. doi: 10.1007/s10566-010-9125-3. PMID: 2011-06151-001. Exclusion Code: X2.
- 229. Gittelman-Klein R, Klein DF. School phobia: diagnostic considerations in the light of imipramine effects. J Nerv Ment Dis. 1973 Mar;156(3):199-215. PMID: 4698665. Exclusion Code: X3.
- 230. Gladstone T, Terrizzi D, Stinson A, et al. Effect of internet-based cognitive behavioral humanistic and interpersonal training vs. internet-based general health education on adolescent depression in primary care: a randomized clinical trial. JAMA Netw Open. 2018 Nov;1(7)doi: 10.1001/jamanetworkopen.2018.4278. PMID: 30533601. Exclusion Code: X2.
- 231. Gladstone TG, Marko-Holguin M, Rothberg P, et al. An internet-based adolescent depression preventive intervention: study protocol for a randomized control trial. Trials. 2015 May 1;16:203. doi: 10.1186/s13063-015-0705-2. PMID: 25927539. Exclusion Code: X2.
- 232. GlaxoSmithKline. A double-blind, multicentre placebo controlled study of paroxetine in adolescents with unipolar major depression.

 1998. http://cochrane/clcentral/articles/038/CN-00497038/frame.html. Exclusion Code: X3.
- 233. Goldbeck L, Ellerkamp T. A randomized controlled trial of multimodal music therapy for children with anxiety disorders. J Music Ther. 2012 Win 2012;49(4):395-413. doi: 10.1093/jmt/49.4.395. PMID: 2013-11365-002. Exclusion Code: X3.
- Goldney RD. Immediate post intervention effects of two brief youth suicide prevention interventions. Suicide Life Threat Behav. 2002 Winter;32(4):454; author reply -6. PMID: 12501969. Exclusion Code: X8.
- 235. Goldschmidt K. Tele-mental health for children: using videoconferencing for Cognitive Behavioral Therapy (CBT). J Pediatr Nurs. 2016 Nov-Dec;31(6):742-4. doi: 10.1016/j.pedn.2016.09.001. PMID: 27726971. Exclusion Code: X3.
- 236. Gonzalez A, Weersing VR, Warnick E, et al. Cross-ethnic measurement equivalence of the SCARED in an outpatient sample of African American and non-Hispanic White youths and parents. J Clin Child Adolesc Psychol. 2012;41(3):361-9. doi:

- 10.1080/15374416.2012.654462. PMID: 22397682. Exclusion Code: X2.
- 237. Goodman R, Ford T, Simmons H, et al. Using the Strengths and Difficulties Questionnaire (SDQ) to screen for child psychiatric disorders in a community sample. Int Rev Psychiatry. 2003 Feb-May;15(1-2):166-72. doi: 10.1080/0954026021000046128. PMID: 12745328. Exclusion Code: X3.
- 238. Goodyer IM, Reynolds S, Barrett B, et al.
 Cognitive behavioural therapy and short-term
 psychoanalytical psychotherapy versus a brief
 psychosocial intervention in adolescents with
 unipolar major depressive disorder (IMPACT): a
 multicentre, pragmatic, observer-blind,
 randomised controlled superiority trial. Lancet
 Psychiatry. 2017 Feb;4(2):109-19. doi:
 10.1016/s2215-0366(16)30378-9. PMID:
 27914903. Exclusion Code: X4.
- 239. Gordon MS, Melvin GA. Do antidepressants make children and adolescents suicidal? J Paediatr Child Health. 2014 Nov;50(11):847-54. doi: 10.1111/jpc.12655. PMID: 24941902. Exclusion Code: X7.
- Göttken T, White LO, Klein AM, et al. Short-term psychoanalytic child therapy for anxious children: a pilot study. Psychotherapy (Chic).
 2014 Mar;51(1):148-58. doi: 10.1037/a0036026.
 PMID: 24635002. Exclusion Code: X3.
- 241. Gottlieb L, Martinovich Z, Meyers KM, et al. Treatment for depression enhances protection: Findings from the Treatment for Adolescents With Depression Study (TADS). Int J Cogn Ther. 2016;9(1):38-56. doi: 10.1521/ijct_2016_09_02. PMID: 2016-22581-003. Exclusion Code: X9.
- 242. Graae F, Milner J, Rizzotto L, et al. Clonazepam in childhood anxiety disorders. J Am Acad Child Adolesc Psychiatry. 1994 Mar-Apr;33(3):372-6. doi: 10.1097/00004583-199403000-00011. PMID: 8169182. Exclusion Code: X3.
- 243. Greenfield B, Larson C, Hechtman L, et al. A rapid-response outpatient model for reducing hospitalization rates among suicidal adolescents. Psychiatr Serv. 2002 Dec;53(12):1574-9. doi: 10.1176/appi.ps.53.12.1574. PMID: 12461218. Exclusion Code: X2.
- 244. Grupp-Phelan J, Stevens J, Boyd S, et al. Effect of a motivational interviewing-based intervention on initiation of mental health treatment and mental health after an emergency department visit among suicidal adolescents: a randomized clinical trial. JAMA Netw Open. 2019 Dec 2;2(12):e1917941. doi: 10.1001/jamanetworkopen.2019.17941. PMID: 31860104. Exclusion Code: X5.
- 245. Grupp-Phelan J, Stevens J, Boyd S, et al. Effect of a motivational interviewing—based intervention on initiation of mental health treatment and mental health after an emergency department visit among suicidal adolescents: a randomized clinical trial. JAMA Network Open. 2019;2(12):e1917941-e. doi:

- 10.1001/jamanetworkopen.2019.17941. PMID: 140472240. Language: English. Entry Date: 20191226. Revision Date: 20200120. Publication Type: Article. Exclusion Code: X5.
- 246. Gunlicks-Stoessel M, Westervelt A, Reigstad K, et al. The role of attachment style in interpersonal psychotherapy for depressed adolescents. Psychother Res. 2019 Jan;29(1):78-85. doi: 10.1080/10503307.2017.1315465. PMID: 28436756. Exclusion Code: X4.
- 247. Gupta S, Gersing KR, Erkanli A, et al. Antidepressant regulatory warnings, prescription patterns, suicidality and other aggressive behaviors in major depressive disorder and anxiety disorders. Psychiatr Q. 2016 Jun;87(2):329-42. doi: 10.1007/s11126-015-9389-8. PMID: 26303613. Exclusion Code: X3.
- 248. Gureje O, Kola L, Oladeji BD, et al. Responding to the challenge of Adolescent Perinatal Depression (RAPiD): protocol for a cluster randomized hybrid trial of psychosocial intervention in primary maternal care. Trials. 2020 Feb 27;21(1):231. doi: 10.1186/s13063-020-4086-9. PMID: 32106885. Exclusion Code: X11.
- 249. Hacker KA, Arsenault LN, Williams S, et al. Mental and behavioral health screening at preventive visits: opportunities for follow-up of patients who are nonadherent with the next preventive visit. J Pediatr. 2011 Apr;158(4):666-71.e2. doi: 10.1016/j.jpeds.2010.09.059. PMID: 21074180. Exclusion Code: X7.
- 250. Hale Iii WW, Raaijmakers QA, van Hoof A, et al. Improving screening cut-off scores for DSM-5 adolescent anxiety disorder symptom dimensions with the screen for child anxiety related emotional disorders. Psychiatry J. 2014;2014:517527. doi: 10.1155/2014/517527. PMID: 24829901. Exclusion Code: X5.
- 251. Halldorsdottir T, Ollendick TH. Long-term outcomes of brief, intensive CBT for specific phobias: the negative impact of ADHD symptoms. J Consult Clin Psychol. 2016 May;84(5):465-71. doi: 10.1037/ccp0000088. PMID: 26900895. Exclusion Code: X2.
- 252. Hallgren M, Kraepelien M, Öjehagen A, et al. Physical exercise and internet-based cognitive-behavioural therapy in the treatment of depression: randomised controlled trial. Br J Psychiatry. 2015 Sep;207(3):227-34. doi: 10.1192/bjp.bp.114.160101. PMID: 26089305. Exclusion Code: X2.
- 253. Hammerton G, Zammit S, Potter R, et al. Validation of a composite of suicide items from the Mood and Feelings Questionnaire (MFQ) in offspring of recurrently depressed parents. Psychiatry Res. 2014 Apr 30;216(1):82-8. doi: 10.1016/j.psychres.2014.01.040. PMID: 24534124. Exclusion Code: X2.
- 254. Hampe E, Noble H, Miller LC, et al. Phobic children one and two years posttreatment. J Abnorm Psychol. 1973 Dec;82(3):446-53. doi:

- 10.1037/h0035377. PMID: 4770914. Exclusion Code: X2.
- 255. Hancock KM, Swain J, Hainsworth CJ, et al. Acceptance and commitment therapy versus cognitive behavior therapy for children with anxiety: outcomes of a randomized controlled trial. J Clin Child Adolesc Psychol. 2018 Mar-Apr;47(2):296-311. doi: 10.1080/15374416.2015.1110822. PMID: 26998803. Exclusion Code: X13.
- 256. Haugen W, Haavet OR, Sirpal MK, et al. Identifying depression among adolescents using three key questions: a validation study in primary care. Br J Gen Pract. 2016 Feb;66(643):e65-70. doi: 10.3399/bjgp16X683461. PMID: 26823267. Exclusion Code: X13.
- 257. Haugland BSM, Haaland Å T, Baste V, et al. Effectiveness of brief and standard school-based cognitive-behavioral interventions for adolescents with anxiety: a randomized noninferiority study. J Am Acad Child Adolesc Psychiatry. 2020 Apr;59(4):552-64.e2. doi: 10.1016/j.jaac.2019.12.003. PMID: 31926224. Exclusion Code: X2.
- 258. Haugland BSM, Hysing M, Hoffart A, et al. Effect of early intervention for anxiety on sleep outcomes in adolescents: a randomized trial. Eur Child Adolesc Psychiatry. 2021 May 7doi: 10.1007/s00787-021-01795-6. PMID: 33961115. Exclusion Code: X2.
- 259. Hayward C, Varady S, Albano AM, et al. Cognitive-behavioral group therapy for social phobia in female adolescents: results of a pilot study. J Am Acad Child Adolesc Psychiatry. 2000 Jun;39(6):721-6. doi: 10.1097/00004583-200006000-00010. PMID: 10846306. Exclusion Code: X2.
- 260. Heiligenstein JH, Hoog SL, Wagner KD, et al. Fluoxetine 40-60 mg versus fluoxetine 20 mg in the treatment of children and adolescents with a less-than-complete response to nine-week treatment with fluoxetine 10-20 mg: a pilot study. J Child Adolesc Psychopharmacol. 2006 Feb-Apr;16(1-2):207-17. doi: 10.1089/cap.2006.16.207. PMID: 16553541. Exclusion Code: X4.
- 261. Heinig I, Pittig A, Richter J, et al. Optimizing exposure-based CBT for anxiety disorders via enhanced extinction: design and methods of a multicentre randomized clinical trial. Int J Methods Psychiatr Res. 2017 Jun;26(2)doi: 10.1002/mpr.1560. PMID: 28322476. Exclusion Code: X4.
- 262. Herbert JD, Gaudiano BA, Rheingold AA, et al. Cognitive behavior therapy for generalized social anxiety disorder in adolescents: a randomized controlled trial. J Anxiety Disord. 2009 Mar;23(2):167-77. doi: 10.1016/j.janxdis.2008.06.004. PMID: 18653310. Exclusion Code: X4.
- 263. Hermans M, Korrelboom K, Visser S. A Dutch version of the Overall Anxiety Severity and

- Impairment Scale (OASIS): Psychometric properties and validation. J Affect Disord. 2015;172:127-32. doi: 10.1016/j.jad.2014.09.033. PMID: 2014-54092-020. Exclusion Code: X2.
- 264. Hetrick SE, McKenzie JE, Bailey AP, et al. New generation antidepressants for depression in children and adolescents: a network meta-analysis. Cochrane Database Syst Rev. 2021 May 24;5(5):Cd013674. doi: 10.1002/14651858.CD013674.pub2. PMID: 34029378. Exclusion Code: X7.
- 265. Hetrick SE, Yuen HP, Bailey E, et al. Internet-based cognitive behavioural therapy for young people with suicide-related behaviour (Reframe-IT): a randomised controlled trial. Evid Based Ment Health. 2017 Aug;20(3):76-82. doi: 10.1136/eb-2017-102719. PMID: 28701336. Exclusion Code: X13.
- 266. Hill RM, Gushanas KL, Alvis L, et al. Geospatial identification of high youth suicide risk areas via electronic health records: Avenues for research and prevention efforts. Suicide Life Threat Behav. 2021 Apr;51(2):255-62. doi: 10.1111/sltb.12701. PMID: 33876482. Exclusion Code: X3.
- 267. Hill RM, Oosterhoff B, Do C. Using machine learning to identify suicide risk: a classification tree approach to prospectively identify adolescent suicide attempters. Arch Suicide Res. 2020 Apr-Jun;24(2):218-35. doi: 10.1080/13811118.2019.1615018. PMID: 31079565. Exclusion Code: X3.
- 268. Hirschtritt ME, Pagano ME, Christian KM, et al. Moderators of fluoxetine treatment response for children and adolescents with comorbid depression and substance use disorders. J Subst Abuse Treat. 2012 Jun;42(4):366-72. doi: 10.1016/j.jsat.2011.09.010. PMID: 22116008. Exclusion Code: X9.
- 269. Hishinuma ES, Miyamoto RH, Nishimura ST, et al. Prediction of anxiety disorders using the state-trait anxiety inventory for multiethnic adolescents. J Anxiety Disord. 2001 Nov-Dec;15(6):511-33. doi: 10.1016/s0887-6185(01)00079-2. PMID: 11764310. Exclusion Code: X3.
- 270. Ho D. Antidepressants and the FDA's black-box warning: determining a rational public policy in the absence of sufficient evidence. Virtual Mentor. 2012 Jun 1;14(6):483-8. doi: 10.1001/virtualmentor.2012.14.6.pfor2-1206. PMID: 23351264. Exclusion Code: X3.
- 271. Högberg C, Billstedt E, Björck C, et al. Diagnostic validity of the MINI-KID disorder classifications in specialized child and adolescent psychiatric outpatient clinics in Sweden. BMC Psychiatry. 2019 May 9;19(1):142. doi: 10.1186/s12888-019-2121-8. PMID: 31072319. Exclusion Code: X3.
- 272. Högberg G, Antonuccio DO, Healy D. Suicidal risk from TADS study was higher than it first appeared. Int J Risk Saf Med. 2015;27(2):85-91.

498

- doi: 10.3233/jrs-150645. PMID: 26410011. Exclusion Code: X8.
- 273. Högberg G, Hällström T. Mood regulation focused CBT based on memory reconsolidation, reduced suicidal ideation and depression in youth in a randomised controlled study. Int J Environ Res Public Health. 2018 May 5;15(5)doi: 10.3390/ijerph15050921. PMID: 29734740. Exclusion Code: X2.
- 274. Holcomb JM, Arauz Boudreau A, Riobueno-Naylor A, et al. Beyond initial screening: one-year follow-up of adolescents with internalizing problems on the pediatric symptom checklist. J Dev Behav Pediatr. 2021 May 1;42(4):283-90. doi: 10.1097/dbp.0000000000000890. PMID: 33908902. Exclusion Code: X4.
- 275. Holi MM, Pelkonen M, Karlsson L, et al.
 Detecting suicidality among adolescent
 outpatients: evaluation of trained clinicians'
 suicidality assessment against a structured
 diagnostic assessment made by trained raters.
 BMC Psychiatry. 2008 Dec 31;8:97. doi:
 10.1186/1471-244x-8-97. PMID: 19116040.
 Exclusion Code: X2.
- 276. Hooper Weatherly A. Effectiveness of two psychiatric screening tools for adolescent suicide risk. Pediatr Nurs. 2019;45(4):180-3. PMID: 138187839. Language: English. Entry Date: 20190824. Revision Date: 20190827. Publication Type: Article. Exclusion Code: X2.
- 277. Hopper SM, Woo JW, Sharwood LN, et al. Prevalence of suicidality in asymptomatic adolescents in the paediatric emergency department and utility of a screening tool. Emerg Med Australas. 2012 Oct;24(5):540-6. doi: 10.1111/j.1742-6723.2012.01576.x. PMID: 23039296. Exclusion Code: X13.
- 278. Horowitz LM, Bridge JA, Teach SJ, et al. Ask Suicide-Screening Questions (ASQ): a brief instrument for the pediatric emergency department. Arch Pediatr Adolesc Med. 2012 Dec;166(12):1170-6. doi: 10.1001/archpediatrics.2012.1276. PMID: 23027429. Exclusion Code: X4.
- 279. Horowitz LM, Mournet AM, Lanzillo E, et al. Screening pediatric medical patients for suicide risk: is depression screening enough? J Adolesc Health. 2021 Jun;68(6):1183-8. doi: 10.1016/j.jadohealth.2021.01.028. PMID: 33712380. Exclusion Code: X2.
- 280. Horowitz LM, Wharff EA, Mournet AM, et al. Validation and feasibility of the ASQ among pediatric medical and surgical inpatients. Hosp Pediatr. 2020 Sep;10(9):750-7. doi: 10.1542/hpeds.2020-0087. PMID: 32826283. Exclusion Code: X5.
- 281. Horton SE, Hughes JL, King JD, et al. Preliminary examination of the interpersonal psychological theory of suicide in an adolescent clinical sample. J Abnorm Child Psychol. 2016;44(6):1133-44. doi: 10.1007/s10802-015-

- 0109-5. PMID: 2015-56893-001. Exclusion Code: X3.
- 282. Horwitz AG, Czyz EK, King CA. Predicting future suicide attempts among adolescent and emerging adult psychiatric emergency patients. J Clin Child Adolesc Psychol. 2015;44(5):751-61. doi: 10.1080/15374416.2014.910789. PMID: 24871489. Exclusion Code: X9.
- 283. Hudson JL, Newall C, Rapee RM, et al. The impact of brief parental anxiety management on child anxiety treatment outcomes: a controlled trial. J Clin Child Adolesc Psychol. 2014;43(3):370-80. doi: 10.1080/15374416.2013.807734. PMID: 23845064. Exclusion Code: X4.
- 284. Hudson JL, Rapee RM, Deveney C, et al.
 Cognitive-behavioral treatment versus an active control for children and adolescents with anxiety disorders: a randomized trial. J Am Acad Child Adolesc Psychiatry. 2009 May;48(5):533-44. doi: 10.1097/CHI.0b013e31819c2401. PMID: 19318990. Exclusion Code: X4.
- 285. Hughes CW, Barnes S, Barnes C, et al. Depressed Adolescents Treated with Exercise (DATE): a pilot randomized controlled trial to test feasibility and establish preliminary effect sizes. Ment Health Phys Act. 2013 Jun;6(2):119-31. doi: 10.1016/j.mhpa.2013.06.006. PMID: 24244220. Exclusion Code: X4.
- 286. Idsoe T, Keles S, Olseth AR, et al. Cognitive behavioral treatment for depressed adolescents: results from a cluster randomized controlled trial of a group course. BMC Psychiatry. 2019 May 22;19(1):155. doi: 10.1186/s12888-019-2134-3. PMID: 31117989. Exclusion Code: X2.
- 287. Iftene F, Predescu E, Stefan S, et al. Rational-emotive and cognitive-behavior therapy (REBT/CBT) versus pharmacotherapy versus REBT/CBT plus pharmacotherapy in the treatment of major depressive disorder in youth; a randomized clinical trial. Psychiatry Res. 2015 Feb 28;225(3):687-94. doi: 10.1016/j.psychres.2014.11.021. PMID: 25500320. Exclusion Code: X4.
- 288. In-Albon T, Dubi K, Rapee RM, et al. Forced choice reaction time paradigm in children with separation anxiety disorder, social phobia, and nonanxious controls. Behav Res Ther. 2009;47(12):1058-65. doi: 10.1016/j.brat.2009.08.003. PMID: 2009-15906-001. Exclusion Code: X2.
- 289. In-Albon T, Meyer AH, Schneider S. Separation Anxiety Avoidance Inventory-Child and Parent Version: Psychometric properties and clinical utility in a clinical and school sample. Child Psychiatry Hum Dev. 2013;44(6):689-97. doi: 10.1007/s10578-013-0364-z. PMID: 2013-04319-001. Exclusion Code: X7.
- 290. Infantino A, Donovan CL, March S. A randomized controlled trial of an audio-based treatment program for child anxiety disorders. Behav Res Ther. 2016 Apr;79:35-45. doi:

499

- 10.1016/j.brat.2016.02.007. PMID: 26950257. Exclusion Code: X13.
- 291. Ingul JM, Aune T, Nordahl HM. A randomized controlled trial of individual cognitive therapy, group cognitive behaviour therapy and attentional placebo adolescent social phobia. Psychother Psychosom. 2014;83(1):54-61. doi: 10.1159/000354672. PMID: 2013-41405-007. Exclusion Code: X13.
- 292. Ingul JM, Aune T, Nordahl HM. A randomized controlled trial of individual cognitive therapy, group cognitive behaviour therapy and attentional placebo for adolescent social phobia. Psychother Psychosom. 2014;83(1):54-61. doi: 10.1159/000354672. PMID: 24281563. Exclusion Code: X10.
- 293. Iorfino F, Ho N, Carpenter JS, et al. Predicting self-harm within six months after initial presentation to youth mental health services: A machine learning study. PLoS One. 2020;15(12):e0243467. doi: 10.1371/journal.pone.0243467. PMID: 33382713. Exclusion Code: X3.
- 294. Ip P, Chim D, Chan KL, et al. Effectiveness of a culturally attuned Internet-based depression prevention program for Chinese adolescents: A randomized controlled trial. Depress Anxiety. 2016;33(12):1123-31. doi: 10.1002/da.22554. PMID: 2016-44415-001. Exclusion Code: X5.
- Isaacs D, Nunn K. Antidepressants and suicide in adolescents. J Paediatr Child Health.
 2014;50(10):836-7. doi: 10.1111/jpc.12718.
 PMID: 2014-42842-022. Exclusion Code: X3.
- 296. Isacsson G, Ahlner J. Antidepressants and the risk of suicide in young persons--prescription trends and toxicological analyses. Acta Psychiatr Scand. 2014 Apr;129(4):296-302. doi: 10.1111/acps.12160. PMID: 23773187. Exclusion Code: X3.
- 297. Isacsson G, Ahlner J. Antidepressants and the risk of suicide in young persons—Prescription trends and toxicological analyses. Acta Psychiatr Scand. 2014;129(4):296-302. doi: 10.1111/acps.12160. PMID: 2014-09600-005. Exclusion Code: X3.
- 298. Ishikawa S, Motomura N, Kawabata Y, et al. Cognitive behavioural therapy for Japanese children and adolescents with anxiety disorders: a pilot study. Behav Cogn Psychother. 2012 May;40(3):271-85. doi: 10.1017/s1352465811000713. PMID: 22217534. Exclusion Code: X4.
- 299. Israel P, Diamond GS. Feasibility of attachment based family therapy for depressed clinic-referred Norwegian adolescents. Clin Child Psychol Psychiatry. 2013;18(3):334-50. doi: 10.1177/1359104512455811. PMID: 108668356. Language: English. Entry Date: 20160426. Revision Date: 20160426. Publication Type: Article. Exclusion Code: X4.
- 300. Ivarsson T, Skarphedinsson G, Andersson M, et al. The validity of the Screen for Child Anxiety

- Related Emotional Disorders Revised (SCARED-R) Scale and Sub-Scales in Swedish youth. Child Psychiatry Hum Dev. 2018 Apr;49(2):234-43. doi: 10.1007/s10578-017-0746-8. PMID: 28756556. Exclusion Code: X5.
- 301. Jacobs RH, Watkins ER, Peters AT, et al.
 Targeting ruminative thinking in adolescents at risk for depressive relapse: rumination-focused cognitive behavior therapy in a pilot randomized controlled trial with resting State fMRI. PLoS One. 2016;11(11):e0163952. doi: 10.1371/journal.pone.0163952. PMID: 27880789. Exclusion Code: X2.
- 302. Jansen M, Bodden DHM, Muris P, et al.
 Measuring anxiety in children: the importance of
 separate mother and father reports. Child Youth
 Care Forum. 2017;46(5):643-59. doi:
 10.1007/s10566-017-9402-5. PMID: 28989266.
 Exclusion Code: X9.
- 303. Jansen M, van Doorn MMEM, Lichtwarck-Aschoff A, et al. Effectiveness of a cognitive-behavioral therapy (CBT) manualized program for clinically anxious children: study protocol of a randomized controlled trial. BMC Psychiatry. 2012;12doi: 10.1186/1471-244X-12-16. PMID: 2012-09160-001. Exclusion Code: X4.
- Jarbin H, Ivarsson T, Andersson M, et al.
 Screening efficiency of the Mood and Feelings
 Questionnaire (MFQ) and Short Mood and
 Feelings Questionnaire (SMFQ) in Swedish help
 seeking outpatients. PLoS One.
 2020;15(3):e0230623. doi:
 10.1371/journal.pone.0230623. PMID:
 32210463. Exclusion Code: X5.
- 305. Jensen PS, Salzberg AD, Richters JE, et al. Scales, diagnoses, and child psychopathology: I. CBCL and DISC relationships. J Am Acad Child Adolesc Psychiatry. 1993 Mar;32(2):397-406. doi: 10.1097/00004583-199303000-00022. PMID: 8444770. Exclusion Code: X9.
- 306. Jensen PS, Watanabe HK, Richters JE, et al. Scales, diagnoses, and child psychopathology: II. Comparing the CBCL and the DISC against external validators. J Abnorm Child Psychol. 1996 Apr;24(2):151-68. doi: 10.1007/bf01441482. PMID: 8743242. Exclusion Code: X7.
- 307. Jensen-Doss A, Ehrenreich-May J, Nanda MM, et al. Community Study of Outcome Monitoring for Emotional Disorders in Teens (COMET): A comparative effectiveness trial of a transdiagnostic treatment and a measurement feedback system. Contemp Clin Trials. 2018 Nov;74:18-24. doi: 10.1016/j.cct.2018.09.011. PMID: 30282056. Exclusion Code: X11.
- 308. Jeppesen P, Wolf RT, Nielsen SM, et al. Effectiveness of transdiagnostic cognitive-behavioral psychotherapy compared with management as usual for youth with common mental health problems: a randomized clinical trial. JAMA Psychiatry. 2021 Mar 1;78(3):250-

- 60. doi: 10.1001/jamapsychiatry.2020.4045. PMID: 33355633. Exclusion Code: X2.
- Joe S, Scott ML, Banks A. What works for adolescent Black males at risk of suicide. Res Soc Work Pract. 2018;28(3):340-5. doi: 10.1177/1049731517702745. PMID: 128090165. Language: English. Entry Date: 20180301. Revision Date: 20180306. Publication Type: Article. Exclusion Code: X7.
- 310. Johnco CJ, Salloum A, Lewin AB, et al. Refining clinical judgment of treatment response and symptom remission identification in childhood anxiety using a signal detection analysis on the Pediatric Anxiety Rating Scale. J Child Adolesc Psychopharmacol. 2015 Nov;25(9):674-83. doi: 10.1089/cap.2015.0102. PMID: 26579629. Exclusion Code: X4.
- 311. Johnson HS, Inderbitzen-Nolan HM, Anderson ER. The social phobia inventory: validity and reliability in an adolescent community sample. Psychol Assess. 2006 Sep;18(3):269-77. doi: 10.1037/1040-3590.18.3.269. PMID: 16953730. Exclusion Code: X13.
- 312. Johnstone JM, Luty SE, Carter JD, et al. Childhood neglect and abuse as predictors of antidepressant response in adult depression. Depress Anxiety. 2009;26(8):711-7. doi: 10.1002/da.20590. PMID: 19544315. Exclusion Code: X2.
- Jonovich SJ, Alpert-Gillis LJ. Impact of pediatric mental health screening on clinical discussion and referral for services. Clin Pediatr (Phila).
 2014 Apr;53(4):364-71. doi: 10.1177/0009922813511146. PMID: 24302536.
 Exclusion Code: X9.
- 314. Joormann J, Unnewehr S. Eine kontrollierte Studie zur Wirksamkeit einer kognitivverhaltenstherapeutischen Gruppentherapie bei Kindern und Jugendlichen mit Sozialer Phobie. Zeitschrift für Klinische Psychologie und Psychotherapie; Forschung und Praxis. 2002;31(4):284-90. Exclusion Code: X1.
- 315. Julious SA. Efficacy and suicidal risk for antidepressants in paediatric and adolescent patients. Stat Methods Med Res. 2013
 Apr;22(2):190-218. doi:
 10.1177/0962280211432210. PMID: 22267546.
 Exclusion Code: X7.
- 316. Kaess M, Edinger A, Fischer-Waldschmidt G, et al. Effectiveness of a brief psychotherapeutic intervention compared with treatment as usual for adolescent nonsuicidal self-injury: a single-centre, randomised controlled trial. Eur Child Adolesc Psychiatry. 2020 Jun;29(6):881-91. doi: 10.1007/s00787-019-01399-1. PMID: 31512050. Exclusion Code: X2.
- 317. Kaess M, Koenig J, Bauer S, et al. Self-injury: Treatment, Assessment, Recovery (STAR): online intervention for adolescent non-suicidal self-injury - study protocol for a randomized controlled trial. Trials. 2019 Jul 12;20(1):425.

- doi: 10.1186/s13063-019-3501-6. PMID: 31300065. Exclusion Code: X11.
- 318. Kaess M, Schnyder N, Michel C, et al. Twelvemonth service use, suicidality and mental health problems of European adolescents after a schoolbased screening for current suicidality. Eur Child Adolesc Psychiatry. 2020 Dec 15doi: 10.1007/s00787-020-01681-7. PMID: 33320300. Exclusion Code: X9.
- 319. Kampmann IL, Emmelkamp PM, Hartanto D, et al. Exposure to virtual social interactions in the treatment of social anxiety disorder: A randomized controlled trial. Behav Res Ther. 2016 Feb;77:147-56. doi: 10.1016/j.brat.2015.12.016. PMID: 26752328. Exclusion Code: X2.
- 320. Kantor JE, Walker CE, Hays L. A study of the usefulness of Lanyon's Psychological Screening Inventory with adolescents. J Consult Clin Psychol. 1976 Jun;44(3):313-6. doi: 10.1037//0022-006x.44.3.313. PMID: 932260. Exclusion Code: X3.
- 321. Karabekiroglu K, Karakurt MN, Yuce M, et al. Fluoxetine for the Treatment of Childhood and Adolescence Social Phobia: Factors playing a role in Efficacy. Klinik Psikofarmakoloji Bülteni-Bulletin of Clinical Psychopharmacology. 2011;21(4):317-24. Exclusion Code: X4.
- 322. Katon W, Russo J, Richardson L, et al. Anxiety and depression screening for youth in a primary care population. Ambul Pediatr. 2008 May-Jun;8(3):182-8. doi: 10.1016/j.ambp.2008.01.003. PMID: 18501865. Exclusion Code: X13.
- 323. Keeton CP, Caporino NE, Kendall PC, et al. Mood and suicidality outcomes 3–11 years following pediatric anxiety disorder treatment. Depress Anxiety. 2019;36(10):930-40. doi: 10.1002/da.22944. PMID: 2019-44452-001. Exclusion Code: X9.
- 324. Keeton CP, Ginsburg GS, Drake KL, et al.
 Benefits of child-focused anxiety treatments for
 parents and family functioning. Depress Anxiety.
 2013 Sep;30(9):865-72. doi: 10.1002/da.22055.
 PMID: 23390005. Exclusion Code: X9.
- 325. Keles S, Idsoe T. Six- and twelve-month followup results of a cluster randomized controlled trial of a CBT-based group course. Prev Sci. 2021 May;22(4):409-18. doi: 10.1007/s11121-020-01160-0. PMID: 32889703. Exclusion Code: X2.
- 326. Keller MB, Ryan ND, Strober M, et al. Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. J Am Acad Child Adolesc Psychiatry. 2001
 Jul;40(7):762-72. doi: 10.1097/00004583-200107000-00010. PMID: 11437014. Exclusion Code: X3.
- 327. Kendall PC. Treating anxiety disorders in children: results of a randomized clinical trial. J Consult Clin Psychol. 1994;62(1):100. Exclusion Code: X13.

- 328. Kendall PC, Cummings CM, Villabø MA, et al. Mediators of change in the Child/Adolescent Anxiety Multimodal Treatment Study. J Consult Clin Psychol. 2016 Jan;84(1):1-14. doi: 10.1037/a0039773. PMID: 26460572. Exclusion Code: X9
- 329. Kendall PC, Flannery-Schroeder E, Panichelli-Mindel SM, et al. Therapy for youths with anxiety disorders: a second randomized clinical trial. J Consult Clin Psychol. 1997 Jun;65(3):366-80. doi: 10.1037//0022-006x.65.3.366. PMID: 9170760. Exclusion Code: X13.
- 330. Kendall PC, Hudson JL, Gosch E, et al.
 Cognitive-behavioral therapy for anxiety
 disordered youth: A randomized clinical trial
 evaluating child and family modalities. J Consult
 Clin Psychol. 2008;76(2):282-97. doi:
 10.1037/0022-006X.76.2.282. PMID: 200803290-010. Exclusion Code: X4.
- 331. Kennard BD, Emslie GJ, Mayes TL, et al. Sequential treatment with fluoxetine and relapse-prevention CBT to improve outcomes in pediatric depression. Am J Psychiatry. 2014 Oct;171(10):1083-90. doi: 10.1176/appi.ajp.2014.13111460. PMID: 24935082. Exclusion Code: X3.
- 332. Kennard BD, Emslie GJ, Mayes TL, et al.
 Cognitive-behavioral therapy to prevent relapse in pediatric responders to pharmacotherapy for major depressive disorder. J Am Acad Child Adolesc Psychiatry. 2008 Dec;47(12):1395-404. doi: 10.1097/CHI.0b013e31818914a1. PMID: 18978634. Exclusion Code: X2.
- 333. Kennard BD, Mayes TL, Chahal Z, et al.
 Predictors and moderators of relapse in children
 and adolescents with major depressive disorder. J
 Clin Psychiatry. 2018 Mar/Apr;79(2)doi:
 10.4088/JCP.15m10330. PMID: 29474007.
 Exclusion Code: X9.
- 334. Kent L, Vostanis P, Feehan C. Detection of major and minor depression in children and adolescents: evaluation of the Mood and Feelings Questionnaire. J Child Psychol Psychiatry. 1997 Jul;38(5):565-73. doi: 10.1111/j.1469-7610.1997.tb01543.x. PMID: 9255700. Exclusion Code: X2.
- 335. Kerker BD, Chor KH, Hoagwood KE, et al. Detection and treatment of mental health issues by pediatric PCPs in New York State: an evaluation of Project TEACH. Psychiatr Serv. 2015 Apr 1;66(4):430-3. doi: 10.1176/appi.ps.201400079. PMID: 25828984. Exclusion Code: X9.
- 336. Kersun LS, Shemesh E. Depression and anxiety in children at the end of life. Pediatr Clin North Am. 2007 Oct;54(5):691-708, xi. doi: 10.1016/j.pcl.2007.06.003. PMID: 17933618. Exclusion Code: X8.
- 337. Khanna MS, Kendall PC. Computer-assisted cognitive behavioral therapy for child anxiety: results of a randomized clinical trial. J Consult Clin Psychol. 2010;78(5):737-45. doi:

- 10.1037/a0019739. PMID: 2010-19874-014. Exclusion Code: X13.
- 338. Kim SM, Han DH, Lee YS, et al. Combined cognitive behavioral therapy and bupropion for the treatment of problematic on-line game play in adolescents with major depressive disorder.

 Comput Human Behav. 2012;28(5):1954-9.
 PMID: CN-00853199. Exclusion Code: X3.
- 339. King CA, Brent D, Grupp-Phelan J, et al. Prospective Development and Validation of the Computerized Adaptive Screen for Suicidal Youth. JAMA Psychiatry. 2021 May 1;78(5):540-9. doi: 10.1001/jamapsychiatry.2020.4576. PMID: 33533908. Exclusion Code: X4.
- 340. King CA, Kramer A, Preuss L, et al. Youth-Nominated Support Team for Suicidal Adolescents (Version 1): a randomized controlled trial. J Consult Clin Psychol. 2006 Feb;74(1):199-206. doi: 10.1037/0022-006x.74.1.199. PMID: 16551158. Exclusion Code: X2.
- 341. King CD, Joyce VW, Kleiman EM, et al.
 Relevance of the interpersonal theory of suicide
 in an adolescent psychiatric inpatient population.
 Psychiatry Res. 2019 Nov;281:112590. doi:
 10.1016/j.psychres.2019.112590. PMID:
 31634732. Exclusion Code: X9.
- 342. Kitchen CEW, Tiffin PA, Lewis S, et al.
 Innovations in Practice: A randomised controlled
 feasibility trial of Behavioural Activation as a
 treatment for young people with depression.
 Child Adolesc Ment Health. 2020 Jul 28doi:
 10.1111/camh.12415. PMID: 32725758.
 Exclusion Code: X4.
- 343. Klein AM, Rapee RM, Hudson JL, et al.
 Interpretation modification training reduces
 social anxiety in clinically anxious children.
 Behav Res Ther. 2015 Dec;75:78-84. doi:
 10.1016/j.brat.2015.10.006. PMID: 26580081.
 Exclusion Code: X4.
- 344. Klein DN, Arnow BA, Barkin JL, et al. Early adversity in chronic depression: clinical correlates and response to pharmacotherapy. Depress Anxiety. 2009;26(8):701-10. doi: 10.1002/da.20577. PMID: 19434623. Exclusion Code: X2.
- 345. Klein RG, Koplewicz HS, Kanner A. Imipramine treatment of children with separation anxiety disorder. J Am Acad Child Adolesc Psychiatry. 1992 Jan;31(1):21-8. doi: 10.1097/00004583-199201000-00005. PMID: 1347039. Exclusion Code: X3.
- 346. Klein RG, Mannuzza S, Koplewicz HS, et al. Adolescent depression: controlled desipramine treatment and atypical features. Depress Anxiety. 1998;7(1):15-31. PMID: 9592629. Exclusion Code: X3.
- 347. Knepley MJ, Kendall PC, Carper MM. An analysis of the Child Behavior Checklist Anxiety Problems Scale's predictive capabilities. J Psychopathol Behav Assess. 2019 Jun;41(2):249-

- 56. doi: 10.1007/s10862-019-09722-5. PMID: 31666760. Exclusion Code: X2.
- 348. Kocovski NL, Fleming JE, Blackie RA, et al. Self-help for social anxiety: Randomized controlled trial comparing a mindfulness and acceptance-based approach with a control group. Behav Ther. 2019;50(4):696-709. doi: 10.1016/j.beth.2018.10.007. PMID: 2018-63223-001. Exclusion Code: X2.
- 349. Kodal A, Fjermestad K, Bjelland I, et al. Longterm effectiveness of cognitive behavioral therapy for youth with anxiety disorders. J Anxiety Disord. 2018 Jan;53:58-67. doi: 10.1016/j.janxdis.2017.11.003. PMID: 29195188. Exclusion Code: X4.
- 350. Kohlhoff J, Morgan S, Briggs N, et al. Parent-Child Interaction Therapy with Toddlers: A community-based randomized controlled trial with children aged 14-24 months. J Clin Child Adolesc Psychol. 2020 Feb 20:1-16. doi: 10.1080/15374416.2020.1723599. PMID: 32078379. Exclusion Code: X2.
- 351. Kohtala A, Muotka J, Lappalainen R. What happens after five years?: The long-term effects of a four-session Acceptance and Commitment Therapy delivered by student therapists for depressive symptoms. Journal of Contextual Behavioral Science. 2017;6(2):230-8. doi: 10.1016/j.jcbs.2017.03.003. PMID: 2017-23116-016. Exclusion Code: X2.
- 352. Kolko DJ, Campo J, Kilbourne AM, et al. Collaborative care outcomes for pediatric behavioral health problems: A cluster randomized trial. Pediatrics. 2014;133(4):e981-e92. doi: 10.1542/peds.2013-2516. PMID: 2014-12692-007. Exclusion Code: X2.
- 353. Kozina A. School-based prevention of anxiety using the "My FRIENDS" emotional resilience program: Six-month follow-up. Int J Psychol. 2020 Jan;55 Suppl 1:70-7. doi: 10.1002/ijop.12553. PMID: 30511384. Exclusion Code: X2.
- 354. Kratochvil C, Emslie G, Silva S, et al. Acute time to response in the Treatment for Adolescents with Depression Study (TADS). J Am Acad Child Adolesc Psychiatry. 2006 Dec;45(12):1412-8. doi: 10.1097/01.chi.0000237710.73755.14. PMID: 17135986. Exclusion Code: X9.
- 355. Kratochvil CJ, May DE, Silva SG, et al.
 Treatment response in depressed adolescents with and without co-morbid attention-deficit/hyperactivity disorder in the Treatment for Adolescents with Depression Study. J Child Adolesc Psychopharmacol. 2009 Oct;19(5):519-27. doi: 10.1089/cap.2008.0143. PMID: 19877976. Exclusion Code: X4.
- 356. Krause KR, Bear HA, Edbrooke-Childs J, et al. Review: What outcomes count? a review of outcomes measured for adolescent depression between 2007 and 2017. J Am Acad Child Adolesc Psychiatry. 2019 Jan;58(1):61-71. doi:

- 10.1016/j.jaac.2018.07.893. PMID: 30577940. Exclusion Code: X8.
- 357. Kumara H, Kumar V. Impact of Cognitive Behavior Therapy on anxiety and depression in adolescent students. Journal of Psychosocial Research. 2016;11(1):77-85. PMID: 2016-32553-008. Exclusion Code: X2.
- 358. Kye CH, Waterman GS, Ryan ND, et al. A randomized, controlled trial of amitriptyline in the acute treatment of adolescent major depression. J Am Acad Child Adolesc Psychiatry. 1996 Sep;35(9):1139-44. doi: 10.1097/00004583-199609000-00011. PMID: 8824057. Exclusion Code: X3.
- 359. Langer DA, Wood JJ, Bergman RL, et al. A multitrait—multimethod analysis of the construct validity of child anxiety disorders in a clinical sample. Child Psychiatry Hum Dev. 2010;41(5):549-61. doi: 10.1007/s10578-010-0187-0. PMID: 2010-16653-007. Exclusion Code: X9.
- 360. Langley AK, Bergman RL, McCracken J, et al. Impairment in Childhood Anxiety Disorders: Preliminary Examination of the Child Anxiety Impact Scale-Parent Version. J Child Adolesc Psychopharmacol. 2004 Spr 2004;14(1):105-14. doi: 10.1089/104454604773840544. PMID: 2004-14085-015. Exclusion Code: X9.
- 361. Langner TS, Gersten JC, McCarthy ED, et al. A screening inventory for assessing psychiatric impairment in children 6 to 18. J Consult Clin Psychol. 1976 Apr;44(2):286-96. doi: 10.1037//0022-006x.44.2.286. PMID: 1254763. Exclusion Code: X4.
- 362. Last CG, Hansen C, Franco N. Cognitive-behavioral treatment of school phobia. J Am Acad Child Adolesc Psychiatry. 1998 Apr;37(4):404-11. doi: 10.1097/00004583-199804000-00018. PMID: 9549961. Exclusion Code: X13.
- 363. Laurent J, Hadler JR, Stark KD. A multiple-stage screening procedure for the identification of childhood anxiety disorders. Sch Psychol Q. 1994 Win 1994;9(4):239-55. doi: 10.1037/h0088291. PMID: 1995-33371-001. Exclusion Code: X2.
- 364. Le Noury J, Nardo JM, Healy D, et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. BMJ. 2015 Sep 16;351:h4320. doi: 10.1136/bmj.h4320. PMID: 26376805. Exclusion Code: X3.
- 365. Le Noury J, Nardo JM, Healy D, et al. Study 329 continuation phase: Safety and efficacy of paroxetine and imipramine in extended treatment of adolescent major depression. Int J Risk Saf Med. 2016 Sep 17;28(3):143-61. doi: 10.3233/jrs-160728. PMID: 27662279. Exclusion Code; Y3
- 366. Le T, Gobert J. Translating and Implementing a Mindfulness-Based Youth Suicide Prevention Intervention in a Native American Community. Journal of Child & Family Studies.

- 2015;24(1):12-23. doi: 10.1007/s10826-013-9809-z. PMID: 103870905. Language: English. Entry Date: 20150108. Revision Date: 20150710. Publication Type: Journal Article. Exclusion Code: X4
- 367. Lee CS, Williamson LR, Martin SE, et al. Adverse events in very young children prescribed psychotropic medications: Preliminary findings from an acute clinical sample. J Child Adolesc Psychopharmacol. 2015;25(6):509-13. doi: 10.1089/cap.2015.0034. PMID: 2015-37545-008. Exclusion Code: X2.
- 368. Lee H, Zerr A, Dickerson JF, et al. Brief behavioral therapy for anxiety and depression in pediatric primary care: uptake of intervention and community services by ethnic minority families. Journal of the american academy of child and adolescent psychiatry. Conference: 63rd annual meeting of the american academy of child and adolescent psychiatry. United states. Conference start: 20161024. Conference end: 20161029. 2016;55(10 Supplement 1):S181. doi: 10.1016/j.jaac.2016.09.252. PMID: CN-01304638. Exclusion Code: X9.
- 369. Leenarts LE, Dölitzsch C, Schmeck K, et al. Relationship between Massachusetts Youth Screening Instrument-second version and psychiatric disorders in youths in welfare and juvenile justice institutions in Switzerland. BMC Psychiatry. 2016 Sep 30;16(1):340. doi: 10.1186/s12888-016-1032-1. PMID: 27716175. Exclusion Code: X3.
- 370. Leikanger E, Larsson B. One-year stability, change and incidence in anxiety symptoms among early adolescents in the general population. Eur Child Adolesc Psychiatry. 2012 Sep;21(9):493-501. doi: 10.1007/s00787-012-0284-7. PMID: 22562142. Exclusion Code: X3.
- 371. LeMoult J, Colich N, Joormann J, et al. Interpretation bias training in depressed adolescents: near- and far-transfer effects. J Abnorm Child Psychol. 2018 Jan;46(1):159-67. doi: 10.1007/s10802-017-0285-6. PMID: 28299526. Exclusion Code: X4.
- 372. Lepola U, Leinonen E, Koponen H. Citalopram in the treatment of early-onset panic disorder and school phobia. Pharmacopsychiatry. 1996 Jan;29(1):30-2. doi: 10.1055/s-2007-979539. PMID: 8852532. Exclusion Code: X3.
- 373. Leslie KR, Chike-Harris K. Patient-administered screening tool may improve detection and diagnosis of depression among adolescents. Clin Pediatr (Phila). 2018 Apr;57(4):457-60. doi: 10.1177/0009922817730343. PMID: 28950718. Exclusion Code: X9.
- 374. Lewandowski RE, O'Connor B, Bertagnolli A, et al. Screening for and diagnosis of depression among adolescents in a large health Maintenance organization. Psychiatr Serv. 2016 Jun 1;67(6):636-41. doi: 10.1176/appi.ps.201400465. PMID: 26876655. Exclusion Code: X4.

- 375. Lewis CC, Simons AD, Nguyen LJ, et al. Impact of childhood trauma on treatment outcome in the Treatment for Adolescents with Depression Study (TADS). J Am Acad Child Adolesc Psychiatry. 2010 Feb;49(2):132-40. doi: 10.1097/00004583-201002000-00007. PMID: 20215935. Exclusion Code: X9.
- 376. Liber JM, Widenfelt BM, Leeden AJM, et al. The relation of severity and comorbidity to treatment outcome with cognitive behavioral therapy for childhood anxiety disorders. J Abnorm Child Psychol. 2010;38(5):683-94. doi: 10.1007/s10802-010-9394-1. PMID: 2010-11658-011. Exclusion Code: X4.
- 377. Lieberman AF, Ghosh Ippen C, P VANH. Child-parent psychotherapy: 6-month follow-up of a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2006 Aug;45(8):913-8. doi: 10.1097/01.chi.0000222784.03735.92. PMID: 16865033. Exclusion Code: X4.
- 378. Linetzky M, Kahn M, Lazarov A, et al. Gaze-contingent music reward therapy for clinically anxious 7- to 10-year-olds: An open multiple baseline feasibility study. J Clin Child Adolesc Psychol. 2020;49(5):618-25. doi: 10.1080/15374416.2019.1573685. PMID: 2019-17132-001. Exclusion Code: X3.
- 379. Lish JD, Weissman MM, Adams PB, et al. Family psychiatric screening instruments for epidemiologic studies: pilot testing and validation. Psychiatry Res. 1995 Jul 28;57(2):169-80. doi: 10.1016/0165-1781(95)02632-7. PMID: 7480383. Exclusion Code: X3.
- 380. Lois BH, Urban TH, Wong C, et al. Integrating Suicide Risk Screening into Pediatric Ambulatory Subspecialty Care. Pediatr Qual Saf. 2020 May-Jun;5(3):e310. doi: 10.1097/pq9.000000000000310. PMID: 32656472. Exclusion Code: X4.
- 381. Looyeh MY, Kamali K, Ghasemi A, et al.
 Treating social phobia in children through group
 narrative therapy. The arts in psychotherapy.
 2014;41(1):16-20. Exclusion Code: X3.
- 382. Lorentzen V, Fagermo K, Handegård BH, et al. A randomized controlled trial of a six-session cognitive behavioral treatment of emotional disorders in adolescents 14-17 years old in child and adolescent mental health services (CAMHS). BMC Psychol. 2020 Mar 14;8(1):25. doi: 10.1186/s40359-020-0393-x. PMID: 32171328. Exclusion Code: X2.
- 383. Lorenzo-Luaces L, Rodriguez-Quintana N, Bailey AJ. Double trouble: Do symptom severity and duration interact to predicting treatment outcomes in adolescent depression? Behav Res Ther. 2020 Aug;131:103637. doi: 10.1016/j.brat.2020.103637. PMID: 32413595. Exclusion Code: X9.
- 384. Loucas CE, Sclare I, Stahl D, et al. Feasibility randomized controlled trial of a one-day CBT workshop ('DISCOVER') for 15- to 18-year-olds

- with anxiety and/or depression in clinic settings. Behav Cogn Psychother. 2020 Mar;48(2):142-59. doi: 10.1017/s1352465819000286. PMID: 31106728. Exclusion Code: X2.
- 385. Lu L, Mills JA, Li H, et al. Acute
 Neurofunctional Effects of Escitalopram in
 Pediatric Anxiety: A Double-Blind, PlaceboControlled Trial. J Am Acad Child Adolesc
 Psychiatry. 2021 Feb 4doi:
 10.1016/j.jaac.2020.11.023. PMID: 33548492.
 Exclusion Code: X9.
- 386. Luby J. A Randomized Controlled Trial of Parent–Child Psychotherapy in Early Childhood Depression. J Am Acad Child Adolesc Psychiatry. 2018;57(10):S289-. doi: 10.1016/j.jaac.2018.07.691. PMID: CN-01653014. Exclusion Code: X8.
- 387. Luby J, Lenze S, Tillman R. A novel early intervention for preschool depression: findings from a pilot randomized controlled trial. J Child Psychol Psychiatry. 2012 Mar;53(3):313-22. doi: 10.1111/j.1469-7610.2011.02483.x. PMID: 22040016. Exclusion Code: X4.
- 388. Luby JL, Gilbert K, Whalen D, et al. The differential contribution of the components of parent-child interaction therapy emotion development for treatment of preschool depression. J Am Acad Child Adolesc Psychiatry. 2019 Jul 31doi: 10.1016/j.jaac.2019.07.937. PMID: 31376501. Exclusion Code: X9.
- 389. Luntamo T, Korpilahti-Leino T, Ristkari T, et al. Internet-assisted cognitive behavioural therapy with telephone coaching for anxious Finnish children aged 10-13 years: study protocol for a randomised controlled trial. BMJ Open. 2021 Jun 23;11(6):e045474. doi: 10.1136/bmjopen-2020-045474. PMID: 34162641. Exclusion Code: X2.
- 390. Lynch FL, Dickerson JF, Rozenman MS, et al.
 Cost-effectiveness of brief behavioral therapy for
 pediatric anxiety and depression in primary care.
 JAMA Netw Open. 2021 Mar 1;4(3):e211778.
 doi: 10.1001/jamanetworkopen.2021.1778.
 PMID: 33720373. Exclusion Code: X7.
- 391. Manassis K, Mendlowitz SL, Scapillato D, et al. Group and individual cognitive-behavioral therapy for childhood anxiety disorders: a randomized trial. J Am Acad Child Adolesc Psychiatry. 2002 Dec;41(12):1423-30. doi: 10.1097/00004583-200212000-00013. PMID: 12447028. Exclusion Code: X3.
- 392. Mancini C, Van Ameringen M, Oakman JM, et al. Serotonergic agents in the treatment of social phobia in children and adolescents: a case series. Depress Anxiety. 1999;10(1):33-9. doi: 10.1002/(sici)1520-6394(1999)10:1<33::aid-da6>3.0.co;2-h. PMID: 10499188. Exclusion Code: X7.
- 393. Mandoki MW, Tapia MR, Tapia MA, et al. Venlafaxine in the treatment of children and adolescents with major depression.
 Psychopharmacol Bull. 1997;33(1):149-54.
 PMID: 9133767. Exclusion Code: X3.

- 394. March JS, Entusah AR, Rynn M, et al. A randomized controlled trial of venlafaxine ER versus placebo in pediatric social anxiety disorder. Biol Psychiatry. 2007 Nov 15;62(10):1149-54. doi: 10.1016/j.biopsych.2007.02.025. PMID: 17553467. Exclusion Code: X3.
- 395. March S, Spence SH, Donovan CL. The efficacy of an internet-based cognitive-behavioral therapy intervention for child anxiety disorders. J Pediatr Psychol. 2009 Jun;34(5):474-87. doi: 10.1093/jpepsy/jsn099. PMID: 18794187. Exclusion Code: X13.
- 396. Martínez V, Rojas G, Martínez P, et al. Computer-Assisted Cognitive-Behavioral Therapy to Treat Adolescents With Depression in Primary Health Care Centers in Santiago, Chile: A Randomized Controlled Trial. Front Psychiatry. 2019;10:552. doi: 10.3389/fpsyt.2019.00552. PMID: 31417440. Exclusion Code: X4.
- 397. Martins Cde S, Motta JV, Quevedo LA, et al. Comparison of two instruments to track depression symptoms during pregnancy in a sample of pregnant teenagers in Southern Brazil. J Affect Disord. 2015 May 15;177:95-100. doi: 10.1016/j.jad.2015.01.051. PMID: 25754606. Exclusion Code: X6.
- 398. Martinsen KD, Rasmussen LMP, Wentzel-Larsen T, et al. Prevention of anxiety and depression in school children: Effectiveness of the transdiagnostic EMOTION program. J Consult Clin Psychol. 2019 Feb;87(2):212-9. doi: 10.1037/ccp0000360. PMID: 30550301. Exclusion Code: X2.
- Masi G, Toni C, Mucci M, et al. Paroxetine in child and adolescent outpatients with panic disorder. J Child Adolesc Psychopharmacol. 2001 Summer;11(2):151-7. doi: 10.1089/104454601750284054. PMID: 11436954. Exclusion Code: X3.
- 400. Masia Warner C, Colognori D, Brice C, et al. Can school counselors deliver cognitivebehavioral treatment for social anxiety effectively? A randomized controlled trial. J Child Psychol Psychiatry. 2016 Nov;57(11):1229-38. doi: 10.1111/jcpp.12550. PMID: 27002215. Exclusion Code: X4.
- 401. Mathyssek CM, Olino TM, Hartman CA, et al. Does the Revised Child Anxiety and Depression Scale (RCADS) measure anxiety symptoms consistently across adolescence? The TRAILS study. Int J Methods Psychiatr Res. 2013 Mar;22(1):27-35. doi: 10.1002/mpr.1380. PMID: 23483654. Exclusion Code: X4.
- 402. Mayne SL, Hannan C, Davis M, et al. COVID-19 and adolescent depression and suicide risk screening outcomes. Pediatrics. 2021 Jun 17doi: 10.1542/peds.2021-051507. PMID: 34140393. Exclusion Code: X9.
- 403. McCarty CA, Zatzick DF, Marcynyszyn LA, et al. Effect of Collaborative Care on Persistent

- Postconcussive Symptoms in Adolescents: A Randomized Clinical Trial. JAMA Netw Open. 2021 Feb 1;4(2):e210207. doi: 10.1001/jamanetworkopen.2021.0207. PMID: 33635325. Exclusion Code: X2.
- 404. McCauley E, Berk MS, Asarnow JR, et al. Efficacy of Dialectical Behavior Therapy for Adolescents at High Risk for Suicide: A Randomized Clinical Trial. JAMA Psychiatry. 2018 Aug 1;75(8):777-85. doi: 10.1001/jamapsychiatry.2018.1109. PMID: 29926087. Exclusion Code: X4.
- 405. McGrath PJ, Lingley-Pottie P, Thurston C, et al. Telephone-based mental health interventions for child disruptive behavior or anxiety disorders: Randomized trials and overall analysis. J Am Acad Child Adolesc Psychiatry. 2011;50(11):1162-72. doi: 10.1016/j.jaac.2011.07.013. PMID: 2011-24630-015. Exclusion Code: X7.
- 406. McLoone JK, Rapee RM. Comparison of an anxiety management program for children implemented at home and school: Lessons learned. School Mental Health: A Multidisciplinary Research and Practice Journal. 2012;4(4):231-42. doi: 10.1007/s12310-012-9088-7. PMID: 2012-31811-005. Exclusion Code: X5.
- 407. McNally Keehn RH, Lincoln AJ, Brown MZ, et al. The Coping Cat program for children with anxiety and autism spectrum disorder: a pilot randomized controlled trial. J Autism Dev Disord. 2013 Jan;43(1):57-67. doi: 10.1007/s10803-012-1541-9. PMID: 22588377. Exclusion Code: X2.
- 408. Mehlum L. Dialectical behavior therapy (DBT) for adolescents with repeated suicidal behavior a randomized controlled study. In press.
 2012PMID: CN-01038538. Exclusion Code: X8.
- 409. Mehlum L, Ramleth RK, Tørmoen AJ, et al.
 Long term effectiveness of dialectical behavior
 therapy versus enhanced usual care for
 adolescents with self-harming and suicidal
 behavior. Journal of Child Psychology &
 Psychiatry. 2019;60(10):1112-22. doi:
 10.1111/jcpp.13077. PMID: 138570161.
 Language: English. Entry Date: 20190914.
 Revision Date: 20190924. Publication Type:
 Article. Exclusion Code: X10.
- 410. Melfsen S, Kühnemund M, Schwieger J, et al.
 Cognitive behavioral therapy of socially phobic
 children focusing on cognition: a randomised
 wait-list control study. Child Adolesc Psychiatry
 Ment Health. 2011 Feb 28;5(1):5. doi:
 10.1186/1753-2000-5-5. PMID: 21356037.
 Exclusion Code: X13.
- 411. Melvin GA, Dudley AL, Gordon MS, et al.
 Augmenting Cognitive Behavior Therapy for
 School Refusal with Fluoxetine: A Randomized
 Controlled Trial. Child Psychiatry Hum Dev.
 2017 Jun;48(3):485-97. doi: 10.1007/s10578-

- 016-0675-y. PMID: 27485100. Exclusion Code: X4
- 412. Melvin GA, Finnin L, Taffe J, et al. Adverse events reported by anxious school refusing adolescents receiving cognitive behavioral therapy with and without fluoxetine. Clin Child Psychol Psychiatry. 2019 Oct;24(4):892-905. doi: 10.1177/1359104518822681. PMID: 30638065. Exclusion Code: X4.
- 413. Melvin GA, Tonge BJ, King NJ, et al. A comparison of cognitive-behavioral therapy, sertraline, and their combination for adolescent depression. J Am Acad Child Adolesc Psychiatry. 2006 Oct;45(10):1151-61. doi: 10.1097/01.chi.0000233157.21925.71. PMID: 17003660. Exclusion Code: X4.
- 414. Mendez X, Orgiles, et al. . Psychological treatment of the phobia of the dark in a game situation: A controlled essay. . Revista de Psicopatologia y Psicologia Clinica. 2003 Dec;8(3):199-210. PMID: 2004-12003-002. Exclusion Code: X1.
- 415. Mendlowitz SL, Manassis K, Bradley S, et al. Cognitive-behavioral group treatments in childhood anxiety disorders: the role of parental involvement. J Am Acad Child Adolesc Psychiatry. 1999 Oct;38(10):1223-9. doi: 10.1097/00004583-199910000-00010. PMID: 10517054. Exclusion Code: X4.
- 416. Mennin DS, Fresco DM, Heimberg RG, et al. Screening for social anxiety disorder in the clinical setting: using the Liebowitz Social Anxiety Scale. J Anxiety Disord. 2002;16(6):661-73. doi: 10.1016/s0887-6185(02)00134-2. PMID: 12405524. Exclusion Code: X2.
- 417. Menzies RG, Clarke JC. A comparison of in vivo and vicarious exposure in the treatment of childhood water phobia. Behav Res Ther. 1993 Jan;31(1):9-15. doi: 10.1016/0005-7967(93)90037-u. PMID: 8093340. Exclusion Code: X2.
- 418. Michalak J, Probst T, Heidenreich T, et al. Mindfulness-Based Cognitive Therapy and a Group Version of the Cognitive Behavioral Analysis System of Psychotherapy for Chronic Depression: follow-Up Data of a Randomized Controlled Trial and the Moderating Role of Childhood Adversities. Psychother Psychosom. 2016;85(6):378-80. doi: 10.1159/000447014. PMID: CN-01342394. Exclusion Code: X2.
- 419. Miché M, Studerus E, Meyer AH, et al. Prospective prediction of suicide attempts in community adolescents and young adults, using regression methods and machine learning. J Affect Disord. 2020;265:570-8. doi: 10.1016/j.jad.2019.11.093. PMID: 2019-74053-001. Exclusion Code: X3.
- 420. Miller IW, Camargo CA, Jr., Arias SA, et al. Suicide Prevention in an Emergency Department Population: The ED-SAFE Study. JAMA Psychiatry. 2017 Jun 1;74(6):563-70. doi:

- 10.1001/jamapsychiatry.2017.0678. PMID: 28456130. Exclusion Code: X7.
- 421. Miller LC, Barrett CL, Hampe E, et al. Comparison of reciprocal inhibition, psychotherapy, and waiting list control for phobic children. J Abnorm Psychol. 1972 Jun;79(3):269-79. doi: 10.1037/h0033224. PMID: 5033367. Exclusion Code: X3.
- 422. Miniati M, Rucci P, Benvenuti A, et al. Clinical characteristics and treatment outcome of depression in patients with and without a history of emotional and physical abuse. J Psychiatr Res. 2010 Apr;44(5):302-9. doi: 10.1016/j.jpsychires.2009.09.008. PMID: 19800634. Exclusion Code: X7.
- 423. Moharreri F, Heydari Yazdi AS. Evaluation of the Effectiveness of the Friends for Life Program on Children's Anxiety and Depression. Iran J Psychiatry. 2017 Oct;12(4):272-80. PMID: 29472954. Exclusion Code: X6.
- 424. Moller C, Petermann, et al. Short- and long-term effects of a cognitive-behavioural training programme for children with social anxiety. [German]. Verhaltenstherapie. . 2011;21(1):15-22. PMID: 2011134836. Exclusion Code: X1.
- 425. Möller EL, Majdandžić M, Craske MG, et al. Dimensional assessment of anxiety disorders in parents and children for DSM-5. Int J Methods Psychiatr Res. 2014;23(3):331-44. doi: 10.1002/mpr.1450. PMID: 2014-25478-001. Exclusion Code: X9.
- 426. Monga S, Rosenbloom BN, Tanha A, et al. Comparison of child-parent and parent-only cognitive-behavioral therapy programs for anxious children aged 5 to 7 years: short- and long-term outcomes. J Am Acad Child Adolesc Psychiatry. 2015 Feb;54(2):138-46. doi: 10.1016/j.jaac.2014.10.008. PMID: 25617254. Exclusion Code: X4.
- 427. Monga S, Young A, Owens M. Evaluating a cognitive behavioral therapy group program for anxious five to seven year old children: a pilot study. Depress Anxiety. 2009;26(3):243-50. doi: 10.1002/da.20551. PMID: 19212972. Exclusion Code: X7.
- 428. Montgomery LE, Finch AJ, Jr. Validity of two measures of anxiety in children. J Abnorm Child Psychol. 1974 Dec;2(4):293-6. doi: 10.1007/bf00919257. PMID: 4463190. Exclusion Code: X2.
- 429. Morthorst B, Krogh J, Erlangsen A, et al. Effect of assertive outreach after suicide attempt in the AID (assertive intervention for deliberate self harm) trial: randomised controlled trial. BMJ. 2012 Aug 22;345:e4972. doi: 10.1136/bmj.e4972. PMID: 22915730. Exclusion Code: X2.
- 430. Mossman SA, Luft MJ, Schroeder HK, et al. The Generalized Anxiety Disorder 7-item scale in adolescents with generalized anxiety disorder: Signal detection and validation. Ann Clin

- Psychiatry. 2017 Nov;29(4):227-34a. PMID: 29069107. Exclusion Code: X2.
- 431. Mufson L, Weissman MM, Moreau D, et al. Efficacy of interpersonal psychotherapy for depressed adolescents. Arch Gen Psychiatry. 1999 Jun;56(6):573-9. PMID: 10359475. Exclusion Code: X13.
- 432. Mufson L, Yanes-Lukin P, Anderson G. A pilot study of Brief IPT-A delivered in primary care. Gen Hosp Psychiatry. 2015 Sep-Oct;37(5):481-4. doi: 10.1016/j.genhosppsych.2015.04.013. PMID: 25997880. Exclusion Code: X7.
- 433. Muris P, Meesters C, Gobel M. Cognitive coping vs Emotional disclosure in the treatment of anxious children: A pilot-study. Cogn Behav Ther. 2002;31(2):59-67. Exclusion Code: X4.
- 434. Muris P, Meesters C, van Melick M. Treatment of childhood anxiety disorders: a preliminary comparison between cognitive-behavioral group therapy and a psychological placebo intervention. J Behav Ther Exp Psychiatry. 2002 SepDec;33(3-4):143-58. doi: 10.1016/s0005-7916(02)00025-3. PMID: 12628633. Exclusion Code: X7.
- 435. Muris P, Merckelbach H, Holdrinet I, et al. Treating phobic children: effects of EMDR versus exposure. J Consult Clin Psychol. 1998 Feb;66(1):193-8. doi: 10.1037//0022-006x.66.1.193. PMID: 9489274. Exclusion Code: X2
- 436. Muris P, Steerneman P. The Revised version of the Screen for Child Anxiety Related Emotional Disorders (SCARED–R): First evidence for its reliability and validity in a clinical sample. Br J Clin Psychol. 2001;40(1):35-44. doi: 10.1348/014466501163463. PMID: 2001-06105-003. Exclusion Code: X2.
- 437. Mychailyszyn MP, Carper MM, Gibby B.
 Exploring the occurrence of sudden gains among anxious youth receiving evidence-based cognitive-behavioral therapy. Child Adolesc Ment Health. 2018;23(3):251-7. doi: 10.1111/camh.12254. PMID: 2017-53514-001. Exclusion Code: X9.
- 438. Myers MG, Stein MB, Aarons GA. Cross validation of the Social Anxiety Scale for Adolescents in a high school sample. J Anxiety Disord. 2002;16(2):221-32. doi: 10.1016/s0887-6185(02)00098-1. PMID: 12194546. Exclusion Code: X9.
- 439. Academic impairment and impact of treatments among youth with anxiety disorders. Child & Youth Care Forum; 2015. Springer; 44. Exclusion Code: X9.
- 440. Nauta MH, Scholing A, Emmelkamp PM, et al. Cognitive-behavioural therapy for anxiety disordered children in a clinical setting: does additional cognitive parent training enhance treatment effectiveness? Clinical Psychology & Psychotherapy: An International Journal of Theory & Practice. 2001;8(5):330-40. Exclusion Code: X4.

- 441. Nauta MH, Scholing A, Emmelkamp PM, et al. Cognitive-behavioral therapy for children with anxiety disorders in a clinical setting: no additional effect of a cognitive parent training. J Am Acad Child Adolesc Psychiatry. 2003 Nov;42(11):1270-8. doi: 10.1097/01.chi.0000085752.71002.93. PMID: 14566163. Exclusion Code: X13.
- 442. Nauta MH, Scholing A, Rapee RM, et al. A parent-report measure of children's anxiety: psychometric properties and comparison with child-report in a clinic and normal sample. Behav Res Ther. 2004 Jul;42(7):813-39. doi: 10.1016/s0005-7967(03)00200-6. PMID: 15149901. Exclusion Code: X2.
- 443. Navarro MC, Ouellet-Morin I, Geoffroy MC, et al. Machine Learning Assessment of Early Life Factors Predicting Suicide Attempt in Adolescence or Young Adulthood. JAMA Netw Open. 2021 Mar 1;4(3):e211450. doi: 10.1001/jamanetworkopen.2021.1450. PMID: 33710292. Exclusion Code: X3.
- 444. Nelson EL. Cognitive behavioral therapy for childhood depression: a comparison of face-toface and interactive televideo settings. Diss Abstr Int. 2004;65(3-b):1558. PMID: CN-00508148. Exclusion Code: X4.
- 445. Nemeroff CB, Heim CM, Thase ME, et al.
 Differential responses to psychotherapy versus
 pharmacotherapy in patients with chronic forms
 of major depression and childhood trauma. Proc
 Natl Acad Sci U S A. 2003 Nov
 25;100(24):14293-6. doi:
 10.1073/pnas.2336126100. PMID: 14615578.
 Exclusion Code: X7.
- 446. Nemets H, Nemets B, Apter A, et al. Omega-3 treatment of childhood depression: a controlled, double-blind pilot study. Am J Psychiatry. 2006 Jun;163(6):1098-100. doi: 10.1176/ajp.2006.163.6.1098. PMID: 16741212. Exclusion Code: X3.
- 447. Niederer D, Vogt L, Staschke V, et al. Activity trails in the therapy of clinical depression: a randomized controlled equivalence trial. Zeitschrift fur psychosomatische medizin und psychotherapie. 2017;63(2):163-75. doi: 10.13109/zptm.2017.63.2.163. PMID: CN-01410351. Exclusion Code: X1.
- 448. Ntini I, Vadlin S, Olofsdotter S, et al. The Montgomery and Åsberg Depression Rating Scale - self-assessment for use in adolescents: an evaluation of psychometric and diagnostic accuracy. Nord J Psychiatry. 2020 Mar 3:1-8. doi: 10.1080/08039488.2020.1733077. PMID: 32125211. Exclusion Code: X5.
- 449. Núñez D, Arias V, Méndez-Bustos P, et al. Is a brief self-report version of the Columbia severity scale useful for screening suicidal ideation in Chilean adolescents? Compr Psychiatry. 2019 Jan;88:39-48. doi: 10.1016/j.comppsych.2018.11.002. PMID: 30471550. Exclusion Code: X4.

- 450. Oar EL, Farrell LJ, Conlon EG, et al. Patterns of response and remission following a One-Session Treatment for blood-injection-injury phobia in youth. Child Fam Behav Ther. 2017;39(1):43-63. doi: 10.1080/07317107.2016.1268007. PMID: 2017-07104-003. Exclusion Code: X2.
- 451. Obler M, Terwilliger RF. Pilot study on the effectiveness of systematic desensitization with neurologically impaired children with phobic disorders. J Consult Clin Psychol. 1970 Jun;34(3):314-8. doi: 10.1037/h0029367. PMID: 5523436. Exclusion Code: X2.
- 452. O'Brien F, Olden N, Migone M, et al. Group cognitive behavioural therapy for children with anxiety disorder an evaluation of the 'Friends for Youth' programme. Ir J Psychol Med. 2007 Mar;24(1):5-12. doi: 10.1017/s0790966700010065. PMID: 30290497. Exclusion Code: X4.
- 453. O'Connor BC, Lewandowski RE, Rodriguez S, et al. Usual care for adolescent depression from symptom identification through treatment initiation. JAMA Pediatr. 2016 Apr;170(4):373-80. doi: 10.1001/jamapediatrics.2015.4158. PMID: 26832387. Exclusion Code: X3.
- 454. O'Connor E, Gaynes BN, Burda BU, et al. Screening for and treatment of suicide risk relevant to primary care: a systematic review for the U.S. Preventive Services Task Force. Ann Intern Med. 2013 May 21;158(10):741-54. doi: 10.7326/0003-4819-158-10-201305210-00642. PMID: 23609101. Exclusion Code: X7.
- 455. O'Connor K, Bagnell A, McGrath P, et al. An Internet-Based Cognitive Behavioral Program for Adolescents With Anxiety: Pilot Randomized Controlled Trial. JMIR Ment Health. 2020 Jul 24;7(7):e13356. doi: 10.2196/13356. PMID: 32706720. Exclusion Code: X2.
- 456. Odgers K, Dargue N, Creswell C, et al. The limited effect of mindfulness-based interventions on anxiety in children and adolescents: a meta-analysis. Clin Child Fam Psychol Rev. 2020 Sep;23(3):407-26. doi: 10.1007/s10567-020-00319-z. PMID: 32583200. Exclusion Code: X3.
- 457. O'Dor SL, Washburn J, Howard KR, et al. Moderators and Predictors of Response After 36 Weeks of Treatment in the Treatment for Adolescents with Depression Study (TADS). Res Child Adolesc Psychopathol. 2021 May 29doi: 10.1007/s10802-021-00828-7. PMID: 34050856. Exclusion Code: X9.
- 458. O'Keefe VM, Haroz EE, Goklish N, et al.
 Employing a sequential multiple assignment randomized trial (SMART) to evaluate the impact of brief risk and protective factor prevention interventions for American Indian Youth Suicide.
 BMC Public Health. 2019 Dec 12;19(1):1675.
 doi: 10.1186/s12889-019-7996-2. PMID: 31830933. Exclusion Code: X11.
- 459. Oldershaw A, Simic M, Grima E, et al. The effect of cognitive behavior therapy on decision making in adolescents who self-harm: A pilot study.

- Suicide Life Threat Behav. 2012;42(3):255-65. doi: 10.1111/j.1943-278X.2012.0087.x. PMID: 2012-15581-003. Exclusion Code: X7.
- 460. Olivares J, García-López L-J, Beidel DC, et al. Results at long-term among three psychological treatments for adolescents with generalized social phobia (I): Statistical significance. Psicología Conductual. 2002;10(1):147-66. Exclusion Code: X4.
- 461. Olivares J, Olivares-Olivares PJ, Rosa-Alcázar AI, et al. The contribution of the therapist's competence in the treatment of adolescents with generalized social phobia. Psicothema. 2014;26(4):483-9. doi: 10.7334/psicothema2014.69. PMID: 25340895. Exclusion Code: X5.
- 462. Olivares J, Rosa A, Piqueras J. Early detection and treatment of adolescents with generalized social phobia. Psicothema. 2005;17(1):1-8. Exclusion Code: X1.
- 463. Olivares R J, Rosa-Alcazar A, et al. The. The relevance of the individualized attention in the treatment with adolescents under generalized social phobia. International journal of clinical and health psychology. 2006;6(3). Exclusion Code: X1.
- 464. Olivares-Olivares PJ, Rosa-Alcázar AI, Olivares-Rodríguez J. Does individual attention improve the effect of group treatment of adolescents with social phobia? Int J Clin Health Psychol. 2008;8(2):465-81. Exclusion Code: X4.
- 465. Ollendick TH, Halldorsdottir T, Fraire MG, et al. Specific phobias in youth: a randomized controlled trial comparing one-session treatment to a parent-augmented one-session treatment. Behav Ther. 2015 Mar;46(2):141-55. doi: 10.1016/j.beth.2014.09.004. PMID: 25645164. Exclusion Code: X4.
- 466. Ollendick TH, Öst L-G, Reuterskiöld L, et al. One-session treatment of specific phobias in youth: A randomized clinical trial in the United States and Sweden. J Consult Clin Psychol. 2009;77(3):504-16. doi: 10.1037/a0015158. PMID: 2009-08093-012. Exclusion Code: X2.
- 467. Ollendick TH, White SW, Richey J, et al. Attention bias modification treatment for adolescents with social anxiety disorder. Behav Ther. 2019 Jan;50(1):126-39. doi: 10.1016/j.beth.2018.04.002. PMID: 30661553. Exclusion Code: X3.
- 468. Orchard F, Apetroaia A, Clarke K, et al. Cognitive bias modification of interpretation in children with social anxiety disorder. J Anxiety Disord. 2017 Jan;45:1-8. doi: 10.1016/j.janxdis.2016.10.012. PMID: 27866085. Exclusion Code: X3.
- 469. Ortbandt C, Petermann U. Effects of a cognitivebehavioral training program for children with social anxiety. KINDHEIT UND ENTWICKLUNG. 2009;18(1):21-9. Exclusion Code: X1.

- 470. Orvati Aziz M, Mehrinejad SA, Hashemian K, et al. Integrative therapy (short-term psychodynamic psychotherapy & cognitive-behavioral therapy) and cognitive-behavioral therapy in the treatment of generalized anxiety disorder: A randomized controlled trial.

 Complement Ther Clin Pract. 2020

 May;39:101122. doi:
 10.1016/j.ctcp.2020.101122. PMID: 32379661.

 Exclusion Code: X2.
- 471. Ost LG, Svensson L, Hellström K, et al. One-Session treatment of specific phobias in youths: a randomized clinical trial. J Consult Clin Psychol. 2001 Oct;69(5):814-24. PMID: 11680558. Exclusion Code: X2.
- 472. Ougrin D. Adding group psychotherapy to routine care does not improve outcomes in adolescents who repeatedly self-harm. Evid Based Ment Health. 2011 Aug;14(3):84. doi: 10.1136/ebmh.14.3.84. PMID: 21764883. Exclusion Code: X8.
- 473. Ozyurt G, Gencer O, Ozturk Y, et al. Is Triple P effective in childhood anxiety disorder? A randomized controlled study. Psychiatry and clinical psychopharmacology. 2018doi: 10.1080/24750573.2018.1483790. PMID: CN-01645872. Exclusion Code: X6.
- 474. Ozyurt G, Gencer O, Oztürk Y, et al. Long term effectiveness of Triple P Positive Parenting Program on childhood anxiety disorders: a randomised controlled trial. Eur Neuropsychopharmacol. 2014;24:S613-. PMID: CN-01023721. Exclusion Code: X12.
- 475. Özyurt G, Gencer Ö, Öztürk Y, et al. Is triple P positive parenting program effective on anxious children and their parents? 4th month follow up results. J Child Fam Stud. 2016;25(5):1646-55. doi: 10.1007/s10826-015-0343-z. PMID: 2015-57339-001. Exclusion Code: X2.
- 476. Palitz SA, Caporino NE, McGuire JF, et al. Defining treatment response and remission in youth anxiety: a signal detection analysis with the Multidimensional Anxiety Scale for Children. J Am Acad Child Adolesc Psychiatry. 2018 Jun;57(6):418-27. doi: 10.1016/j.jaac.2018.03.013. PMID: 29859557. Exclusion Code: X3.
- 477. Pandya SP. Spiritual counseling program for children with anxiety disorders: a multi-city experiment. J Pastoral Care Counsel. 2018
 Mar;72(1):45-57. doi: 10.1177/1542305018761631. PMID: 29623802. Exclusion Code: X6.
- 478. Papalini S, Lange I, Bakker J, et al. The predictive value of neural reward processing on exposure therapy outcome: Results from a randomized controlled trial. Prog
 Neuropsychopharmacol Biol Psychiatry. 2019
 Jun 8;92:339-46. doi:
 10.1016/j.pnpbp.2019.02.002. PMID: 30763673.
 Exclusion Code: X2.

- 479. Parikh R, Michelson D, Malik K, et al. The effectiveness of a low-intensity problem-solving intervention for common adolescent mental health problems in New Delhi, India: protocol for a school-based, individually randomized controlled trial with an embedded stepped-wedge, cluster randomized controlled recruitment trial. Trials. 2019 Sep 18;20(1):568. doi: 10.1186/s13063-019-3573-3. PMID: 31533783. Exclusion Code: X6.
- 480. Park CH, Kim GS. A validation study on DAS in the prediction of suicidal risk for adolescents. The Arts in Psychotherapy. 2013;40(1):108-14. doi: 10.1016/j.aip.2012.11.006. PMID: 2013-09132-013. Exclusion Code: X9.
- 481. Parker AG, Hetrick SE, Jorm AF, et al. The effectiveness of simple psychological and physical activity interventions for high prevalence mental health problems in young people: A factorial randomised controlled trial. J Affect Disord. 2016 May 15;196:200-9. doi: 10.1016/j.jad.2016.02.043. PMID: 26926659. Exclusion Code: X2.
- 482. Parr CJ, Cartwright-Hatton S. Social anxiety in adolescents: the effect of video feedback on anxiety and the self-evaluation of performance. Clin Psychol Psychother. 2009 Jan-Feb;16(1):46-54. doi: 10.1002/cpp.599. PMID: 19123484. Exclusion Code: X2.
- 483. Paschall MJ, Bersamin M. School-based health centers, depression, and suicide risk among adolescents. Am J Prev Med. 2018 Jan;54(1):44-50. doi: 10.1016/j.amepre.2017.08.022. PMID: 29132951. Exclusion Code: X3.
- 484. Patel A, Watts C, Shiddell S, et al. Universal adolescent suicide screening in a pediatric urgent care center. Arch Suicide Res. 2018 Jan-Mar;22(1):118-27. doi: 10.1080/13811118.2017.1304303. PMID: 28281893. Exclusion Code: X4.
- 485. Pauschardt J, Remschmidt H, Mattejat F.
 Assessing child and adolescent anxiety in
 psychiatric samples with the Child Behavior
 Checklist. J Anxiety Disord. 2010 Jun;24(5):4617. doi: 10.1016/j.janxdis.2010.03.002. PMID:
 20362414. Exclusion Code: X5.
- 486. Pergamin-Hight L, Pine DS, Fox NA, et al. Attention bias modification for youth with social anxiety disorder. J Child Psychol Psychiatry. 2016;57(11):1317-25. doi: 10.1111/jcpp.12599. PMID: 2016-53125-007. Exclusion Code: X3.
- 487. Peris TS, Compton SN, Kendall PC, et al. Trajectories of change in youth anxiety during cognitive—behavior therapy. J Consult Clin Psychol. 2015;83(2):239-52. doi: 10.1037/a0038402, 10.1037/a0038402.supp (Supplemental). PMID: 2014-54663-001. Exclusion Code: X9.
- 488. Peris TS, Sugar CA, Rozenman MS, et al. Longterm service use among youths previously treated for anxiety disorder. J Am Acad Child Adolesc Psychiatry. 2021 Apr;60(4):501-12. doi:

- 10.1016/j.jaac.2020.07.911. PMID: 33301814. Exclusion Code: X9.
- 489. Perloe A, Esposito-Smythers C, Curby TW, et al. Concurrent trajectories of change in adolescent and maternal depressive symptoms in the TORDIA study. J Youth Adolesc. 2014 Apr;43(4):612-28. doi: 10.1007/s10964-013-9999-0. PMID: 23975354. Exclusion Code: X2.
- 490. Perrin S, Last CG. Do childhood anxiety measures measure anxiety? J Abnorm Child Psychol. 1992 Dec;20(6):567-78. doi: 10.1007/bf00911241. PMID: 1487597. Exclusion Code: X5.
- 491. Peterson BS, West AE, Weisz JR, et al. A Sequential Multiple Assignment Randomized Trial (SMART) study of medication and CBT sequencing in the treatment of pediatric anxiety disorders. BMC Psychiatry. 2021 Jun 30;21(1):323. doi: 10.1186/s12888-021-03314-y. PMID: 34193105. Exclusion Code: X4.
- 492. Pettit JW, Bechor M, Rey Y, et al. A Randomized Controlled Trial of Attention Bias Modification Treatment in Youth With Treatment-Resistant Anxiety Disorders. J Am Acad Child Adolesc Psychiatry. 2020 Jan;59(1):157-65. doi: 10.1016/j.jaac.2019.02.018. PMID: 30877049. Exclusion Code: X2.
- 493. Phillips R, Spears MR, Montgomery AA, et al. Could a brief assessment of negative emotions and self-esteem identify adolescents at current and future risk of self-harm in the community? A prospective cohort analysis. BMC Public Health. 2013 Jun 22;13:604. doi: 10.1186/1471-2458-13-604. PMID: 23800153. Exclusion Code: X4.
- 494. Piacentini J, Bennett S, Compton SN, et al. 24and 36-week outcomes for the Child/Adolescent Anxiety Multimodal Study (CAMS). J Am Acad Child Adolesc Psychiatry. 2014;53(3):297-310. doi: 10.1016/j.jaac.2013.11.010. PMID: CN-00982077. Exclusion Code:
- 495. Pina AA, Silverman WK, Fuentes RM, et al. Exposure-based cognitive-behavioral treatment for phobic and anxiety disorders: Treatment effects and maintenance for Hispanic/Latino relative to European-American youths. J Am Acad Child Adolesc Psychiatry. 2003;42(10):1179-87. doi: 10.1097/00004583-200310000-00008. PMID: 2003-08377-006. Exclusion Code: X4.
- 496. Pincus DB, May JE, Whitton SW, et al. Cognitive-behavioral treatment of panic disorder in adolescence. J Clin Child Adolesc Psychol. 2010;39(5):638-49. doi: 10.1080/15374416.2010.501288. PMID: 2010-17041-004. Exclusion Code: X13.
- 497. Posner K, Oquendo MA, Gould M, et al.
 Columbia Classification Algorithm of Suicide
 Assessment (C-CASA): classification of suicidal
 events in the FDA's pediatric suicidal risk
 analysis of antidepressants. Am J Psychiatry.
 2007;164(7):1035-43. doi:

- 10.1176/appi.ajp.164.7.1035. PMID: CN-01772061. Exclusion Code: X2.
- 498. Post P. Impact of child-centered play therapy on the self-esteem, locus of control, and anxiety of at-risk 4th, 5th, and 6th grade students.
 International Journal of Play Therapy.
 1999;8(2):1-18. doi: 10.1037/h0089428. PMID: 2000-13732-001. Exclusion Code: X2.
- 499. Prochaska JD, Le VD, Baillargeon J, et al. Utilization of Professional Mental Health Services Related to Population-Level Screening for Anxiety, Depression, and Post-traumatic Stress Disorder Among Public High School Students. Community Ment Health J. 2016 Aug;52(6):691-700. doi: 10.1007/s10597-015-9968-z. PMID: 26733335. Exclusion Code: X3.
- 500. Putwain DW, Pescod M. Is reducing uncertain control the key to successful test anxiety intervention for secondary school students? Findings from a randomized control trial. Sch Psychol Q. 2018 Jun;33(2):283-92. doi: 10.1037/spq0000228. PMID: 29094957. Exclusion Code: X2.
- 501. Radomski AD, Bagnell A, Curtis S, et al. Examining the Usage, User Experience, and Perceived Impact of an Internet-Based Cognitive Behavioral Therapy Program for Adolescents With Anxiety: Randomized Controlled Trial. JMIR Ment Health. 2020 Feb 7;7(2):e15795. doi: 10.2196/15795. PMID: 32022692. Exclusion Code: X2.
- 502. Randell BP, Eggert LL, Pike KC. Immediate post intervention effects of two brief youth suicide prevention interventions. Suicide Life Threat Behav. 2001 Spring;31(1):41-61. doi: 10.1521/suli.31.1.41.21308. PMID: 11326768. Exclusion Code: X9.
- 503. Rapee RM. Group treatment of children with anxiety disorders: Outcome and predictors of treatment response. Aust J Psychol. 2000;52(3):125-9. Exclusion Code: X7.
- 504. Rapee RM, Abbott MJ, Lyneham HJ.
 Bibliotherapy for children with anxiety disorders using written materials for parents: a randomized controlled trial. J Consult Clin Psychol. 2006
 Jun;74(3):436-44. doi: 10.1037/0022006x.74.3.436. PMID: 16822101. Exclusion Code: X13.
- 505. Rasing SPA, Stikkelbroek YAJ, den Hollander W, et al. Pragmatic Quasi-Experimental Controlled Trial Evaluating the Outcomes of Blended CBT Compared to Face-to-Face CBT and Treatment as Usual for Adolescents with Depressive Disorders. Int J Environ Res Public Health. 2021 Mar 17;18(6)doi: 10.3390/ijerph18063102. PMID: 33802913. Exclusion Code: X2.
- 506. Reardon T, Spence SH, Hesse J, et al. Identifying children with anxiety disorders using brief versions of the Spence Children's Anxiety Scale for children, parents, and teachers. Psychol Assess. 2018 Oct;30(10):1342-55. doi:

- 10.1037/pas0000570. PMID: 29902050. Exclusion Code: X2.
- 507. Reigada LC, Polokowski AR, Walder DJ, et al.
 Treatment for comorbid pediatric gastrointestinal
 and anxiety disorders: A pilot study of a flexible
 health sensitive cognitive-behavioral therapy
 program. Clinical Practice in Pediatric
 Psychology. 2015;3(4):314. Exclusion Code: X2.
- 508. Reinblatt SP, Riddle MA. Selective serotonin reuptake inhibitor-induced apathy: a pediatric case series. J Child Adolesc Psychopharmacol. 2006 Feb-Apr;16(1-2):227-33. doi: 10.1089/cap.2006.16.227. PMID: 16553543. Exclusion Code: X4.
- 509. Renaud J, Birmaher B, Wassick SC, et al. Use of selective serotonin reuptake inhibitors for the treatment of childhood panic disorder: a pilot study. J Child Adolesc Psychopharmacol. 1999;9(2):73-83. doi: 10.1089/cap.1999.9.73.
 PMID: 10461817. Exclusion Code: X4.
- 510. Rengasamy M, Phelps-Tschang J, Simpson M, et al. 6.50 Reduction of Adolescent Suicide Attempts After Telephone-Based Intervention. J Am Acad Child Adolesc Psychiatry. 2018;57(10):S265-. doi: 10.1016/j.jaac.2018.09.411. PMID: CN-01653031. Exclusion Code: X2.
- 511. Reyes-Portillo JA, Chin EM, Toso-Salman J, et al. Using Electronic Health Record Alerts to Increase Safety Planning with Youth At-Risk for Suicide: A Non-randomized Trial. Child & Youth Care Forum. 2018;47(3):391-402. doi: 10.1007/s10566-018-9435-4. PMID: 129180474. Language: English. Entry Date: 20180423. Revision Date: 20190603. Publication Type: Article. Exclusion Code: X7.
- 512. Reyes-Portillo JA, McGlinchey EL, Yanes-Lukin P, et al. Does peer and family interpersonal functioning mediate the impact of interpersonal psychotherapy for latino adolescents in regard to suicidal ideation? J Am Acad Child Adolesc Psychiatry. 2016;55(10):S297-. doi: 10.1016/j.jaac.2016.07.264. PMID: CN-01304636. Exclusion Code: X9.
- 513. Rickhi B, Kania-Richmond A, Moritz S, et al. Evaluation of a spirituality informed e-mental health tool as an intervention for major depressive disorder in adolescents and young adults a randomized controlled pilot trial. BMC Complement Altern Med. 2015 Dec 24;15:450. doi: 10.1186/s12906-015-0968-x. PMID: 26702639. Exclusion Code: X2.
- 514. Rinke ML, German M, Azera B, et al. Effect of Mental Health Screening and Integrated Mental Health on Adolescent Depression-Coded Visits. Clin Pediatr (Phila). 2019 Apr;58(4):437-45. doi: 10.1177/0009922818821889. PMID: 30623684. Exclusion Code: X9.
- 515. Ritter B. The group desensitization of children's snake phobias using vicarious and contact desensitization procedures. Behav Res Ther. 1968 Feb;6(1):1-6. doi: 10.1016/0005-

- 7967(68)90033-8. PMID: 5689466. Exclusion Code: X2.
- 516. Rizo Martínez LE, Guevara Pérez MÁ,
 Hernández González M, et al. A preliminary
 study of the prevalence of post-traumatic stress
 disorder, depression and anxiety symptoms in
 female adolescents maltreatment victims in
 Mexico. Salud Mental. 2018;41(3):139-44. doi:
 10.17711/SM.0185-3325.2018.018. PMID: 201901689-005. Exclusion Code: X6.
- 517. Roaten K, Horowitz LM, Bridge JA, et al.
 Universal Pediatric Suicide Risk Screening in a
 Health Care System: 90,000 Patient Encounters. J
 Acad Consult Liaison Psychiatry. 2021 JulAug;62(4):421-9. doi:
 10.1016/j.jaclp.2020.12.002. PMID: 34219656.
 Exclusion Code: X4.
- 518. Roberts V, Joiner R, Russell C, et al. Mind and Body: an early intervention group programme for adolescents with self-harm thoughts and behaviours. Education & Health. 2019;37(2):46-53. PMID: 137883429. Language: English. Entry Date: 20190807. Revision Date: 20190808. Publication Type: Article. Exclusion Code: X2.
- 519. Robinson J, Hetrick S, Cox G, et al. The development of a randomised controlled trial testing the effects of an online intervention among school students at risk of suicide. BMC Psychiatry. 2014 May 27;14:155. doi: 10.1186/1471-244x-14-155. PMID: 24884888. Exclusion Code: X11.
- 520. Robinson J, Hetrick S, Gook S, et al. Study protocol: the development of a randomised controlled trial testing a postcard intervention designed to reduce suicide risk among young help-seekers. BMC Psychiatry. 2009 Sep 23;9:59. doi: 10.1186/1471-244x-9-59. PMID: 19775469. Exclusion Code: X11.
- 521. Robinson J, Yuen HP, Gook S, et al. Can receipt of a regular postcard reduce suicide-related behaviour in young help seekers? A randomized controlled trial. Early intervention in psychiatry. 2012;6(2):145-52. doi: 10.1111/j.1751-7893.2011.00334.x. PMID: CN-00851791. Exclusion Code: X3.
- 522. Rodrigues Pereira C, Ensink JBM, Güldner MG, et al. Effectiveness of a behavioral treatment protocol for selective mutism in children: Design of a randomized controlled trial. Contemp Clin Trials Commun. 2020 Sep;19:100644. doi: 10.1016/j.conctc.2020.100644. PMID: 32875140. Exclusion Code: X11.
- 523. Roelofs J, Braet C, Rood L, et al. Norms and screening utility of the Dutch version of the Children's Depression Inventory in clinical and nonclinical youths. Psychol Assess. 2010 Dec;22(4):866-77. doi: 10.1037/a0020593. PMID: 21133547. Exclusion Code: X2.
- 524. Rohde P, Clarke GN, Mace DE, et al. An efficacy/effectiveness study of cognitive-behavioral treatment for adolescents with comorbid major depression and conduct disorder.

- J Am Acad Child Adolesc Psychiatry. 2004 Jun;43(6):660-8. doi: 10.1097/01.chi.0000121067.29744.41. PMID: 15167082. Exclusion Code: X2.
- 525. Rohde P, Lewinsohn PM, Seeley JR. Response of depressed adolescents to cognitive-behavioral treatment: do differences in initial severity clarify the comparison of treatments? J Consult Clin Psychol. 1994 Aug;62(4):851-4. PMID: 7962890. Exclusion Code: X4.
- 526. Rohde P, Seeley JR, Kaufman NK, et al.
 Predicting time to recovery among depressed
 adolescents treated in two psychosocial group
 interventions. J Consult Clin Psychol. 2006
 Feb;74(1):80-8. doi: 10.1037/0022-006X.74.1.80.
 PMID: 16551145. Exclusion Code: X2.
- 527. Rojas G, Martínez P, Vöhringer PA, et al.
 Comprehensive technology-assisted training and supervision program to enhance depression management in primary care in Santiago, Chile: study protocol for a cluster randomized controlled trial. Trials. 2015 Jul 24;16:311. doi: 10.1186/s13063-015-0845-4. PMID: 26201546. Exclusion Code: X2.
- 528. Rosa-Alcazar A, Boix M, Olivares-Olivares P. Contributions of cognitive restructuring in the treatment of social phobia in adolescents. Behavioral Psychology/Psicologia Conductual: Revista Internacional Clinica y de la Salud Psicologia Conductual Revista Internacional de Psicologia Clinica de la Salud. 2013;21:6-23. Exclusion Code: X1.
- 529. Rosa-Alcázar A, Olivares-Rodríguez J, Olivares-Olivares P. The role of planned interaction in the treatment of generalized social phobia. Terapia psicológica. 2007;25(2):205-12. Exclusion Code: X1.
- 530. Rossello J, Bernal G. The efficacy of cognitive-behavioral and interpersonal treatments for depression in Puerto Rican adolescents. J Consult Clin Psychol. 1999 Oct;67(5):734-45. PMID: 10535240. Exclusion Code: X13.
- 531. Rossouw T. Mentalisation based treatment for adolescents with self harm: an RCT. Eur Child Adolesc Psychiatry. 2015;24(1 SUPPL. 1):S113. doi: 10.1007/s00787-015-0714-4. PMID: CN-01471379. Exclusion Code: X8.
- 532. Rossow T. Self harm in adolescence, is MBT the answer?: an RCT. Adolescent psychiatry. 2012;2(1):102. PMID: CN-01033258. Exclusion Code: X8.
- 533. Rowe SL, French RS, Henderson C, et al.
 Decisional support for young people who self-harm: protocol for a feasibility trial. BMJ Open.
 2016 Sep 28;6(9):e012161. doi:
 10.1136/bmjopen-2016-012161. PMID:
 27683517. Exclusion Code: X11.
- 534. Rueda-Jaimes GE, Castro-Rueda VA, Rangel-Martínez-Villalba AM, et al. Validity of the Suicidal Behavior Questionnaire-Revised in patients with short-term suicide risk. The European Journal of Psychiatry. 2017;31(4):145-

- 50. doi: 10.1016/j.ejpsy.2017.09.002. PMID: 2019-05498-002. Exclusion Code: X7.
- 535. Rummel-Kluge C, Dietrich S, Koburger N. Behavioural and cognitive-behavioural therapy based self-help versus treatment as usual for depression in adults and adolescents. Cochrane Database Syst Rev. 2015(6)doi: 10.1002/14651858.CD011744. PMID: CD011744. Exclusion Code: X7.
- 536. Rynn MA, Walkup JT, Compton SN, et al. Child/adolescent anxiety multimodal study: evaluating safety. J Am Acad Child Adolesc Psychiatry. 2015;54(3 // () *National Institute of Mental Health*):180-90. doi: 10.1016/j.jaac.2014.12.015. PMID: CN-01077415. Exclusion Code: X9.
- 537. Rytwinski NK, Fresco DM, Heimberg RG, et al. Screening for social anxiety disorder with the self-report version of the Liebowitz Social Anxiety Scale. Depress Anxiety. 2009;26(1):34-8. doi: 10.1002/da.20503. PMID: 18781659. Exclusion Code: X2.
- 538. Saavedra LM, Silverman WK, Morgan-Lopez AA, et al. Cognitive behavioral treatment for childhood anxiety disorders: Long-term effects on anxiety and secondary disorders in young adulthood. J Child Psychol Psychiatry. 2010;51(8):924-34. doi: 10.1111/j.1469-7610.2010.02242.x. PMID: 2010-14446-008. Exclusion Code: x4.
- 539. Sælid GA, Nordahl HM, Rational emotive behaviour therapy in high schools to educate in mental health and empower youth health. A randomized controlled study of a brief intervention. Cogn Behav Ther. 2017 Apr;46(3):196-210. doi: 10.1080/16506073.2016.1233453. PMID: 27791532. Exclusion Code: X5.
- 540. Sakado K, Sato T, Uehara T, et al. Perceived parenting pattern and response to antidepressants in patients with major depression. J Affect Disord. 1999 Jan-Mar;52(1-3):59-66. doi: 10.1016/s0165-0327(98)00062-7. PMID: 10357018. Exclusion Code: X3.
- Sakolsky D. Impact of selective serotonin 541. reuptake inhibitor (SSRI) use on suicidal ideation and behavior in child/adolescent anxiety multimodal extended long-term study. J Am Acad Child Adolesc Psychiatry. 2017;56(10):S319-. doi: 10.1016/j.jaac.2017.07.641. PMID: CN-01452262. Exclusion Code: X8.
- Salari E. Shahriyar Z. Mahmoudi-Gharaei J. et al. 542. Parent-only Group Cognitive Behavioral Intervention for Children with Anxiety Disorders: A Control Group Study. J Can Acad Child Adolesc Psychiatry. 2018 Apr;27(2):130-6. PMID: 29662524. Exclusion Code: X6.
- 543. Salazar DM, Ruiz FJ, Ramírez ES, et al. Acceptance and commitment therapy focused on repetitive negative thinking for child depression: A randomized multiple-baseline evaluation. The

- Psychological Record. 2020;70(3):373-86. doi: 10.1007/s40732-019-00362-5. PMID: 2020-00665-001. Exclusion Code: X9.
- 544. Sallee FR, Richman H, Sethuraman G, et al. Clonidine challenge in childhood anxiety disorder. J Am Acad Child Adolesc Psychiatry. 1998 Jun;37(6):655-62. doi: 10.1097/00004583-199806000-00016. PMID: 9628086. Exclusion Code: X3.
- 545. Salloum A, Andel R, Lewin AB, et al. Family accommodation as a predictor of cognitivebehavioral treatment outcome for childhood anxiety. Fam Soc. 2018;99(1):45-55. doi: 10.1177/1044389418756326. PMID: 2018-12524-006. Exclusion Code: X7.
- 546. Salum GA, Petersen CS, Jarros RB, et al. Group Cognitive Behavioral Therapy and Attention Bias Modification for Childhood Anxiety Disorders: A Factorial Randomized Trial of Efficacy. J Child Adolesc Psychopharmacol. 2018 Nov;28(9):620-30. doi: 10.1089/cap.2018.0022. PMID: 29969293. Exclusion Code: X6.
- 547. Sánchez-García R. Olivares J. Intervención temprana en niños y adolescentes con fobia social. Anuario de psicología. 2009;40(1):75-88. Exclusion Code: X1.
- 548. Santacruz I, Méndez FJ, Sánchez-Meca J. Play therapy applied by parents for children with darkness phobia: Comparison of two programmes. Child Fam Behav Ther. 2006;28(1):19-35. Exclusion Code: X2.
- 549. Santamarina-Perez P, Mendez I, Singh MK, et al. Adapted Dialectical Behavior Therapy for Adolescents with a High Risk of Suicide in a Community Clinic: A Pragmatic Randomized Controlled Trial. Suicide Life Threat Behav. 2020 Jan 16doi: 10.1111/sltb.12612. PMID: 31944371. Exclusion Code: X4.
- 550. Santosh P, Gringras P, Baird G, et al. Development and psychometric properties of the parent version of the Profile of Neuropsychiatric Symptoms (PONS) in children and adolescents. BMC Pediatr. 2015 May 19;15:62. doi: 10.1186/s12887-015-0376-x. PMID: 25986431. Exclusion Code: X9.
- Santucci LC, Ehrenreich-May J. A randomized 551. controlled trial of the child anxiety multi-day program (CAMP) for separation anxiety disorder. Child Psychiatry Hum Dev. 2013 Jun;44(3):439-51. doi: 10.1007/s10578-012-0338-6. PMID: 23053618. Exclusion Code: X13.
- 552. Sayal K, Yates N, Spears M, et al. Service use in adolescents at risk of depression and self-harm: prospective longitudinal study. Soc Psychiatry Psychiatr Epidemiol. 2014 Aug;49(8):1231-40. doi: 10.1007/s00127-014-0843-y. PMID: 24570203. Exclusion Code: X5.
- Scharfstein LA, Beidel DC, Finnell LR, et al. Do 553. pharmacological and behavioral interventions differentially affect treatment outcome for children with social phobia? Behav Modif. 2011 Sep;35(5):451-67. doi:

513

- 10.1177/0145445511408590. PMID: 21586501. Exclusion Code: X9.
- 554. Schilling EA, Aseltine RH, Jr., James A. The SOS Suicide Prevention Program: Further Evidence of Efficacy and Effectiveness. Prev Sci. 2016 Feb;17(2):157-66. doi: 10.1007/s11121-015-0594-3. PMID: 26314868. Exclusion Code: X5
- 555. Schleider J, Weisz J. A single-session growth mindset intervention for adolescent anxiety and depression: 9-month outcomes of a randomized trial. J Child Psychol Psychiatry. 2018;59(2):160-70. doi: 10.1111/jcpp.12811. PMID: 2017-41876-001. Exclusion Code: X3.
- 556. Schleider JL, Ginsburg GS, Keeton CP, et al. Parental psychopathology and treatment outcome for anxious youth: Roles of family functioning and caregiver strain. J Consult Clin Psychol. 2015;83(1):213-24. doi: 10.1037/a0037935. PMID: 2014-38356-001. Exclusion Code: X9.
- 557. Schneider S, Blatter-Meunier J, Herren C, et al. Disorder-specific cognitive-behavioral therapy for separation anxiety disorder in young children: a randomized waiting-list-controlled trial. Psychother Psychosom. 2011;80(4):206-15. doi: 10.1159/000323444. PMID: 2011-23503-003. Exclusion Code: X13.
- 558. Schneider S, Blatter-Meunier J, Herren C, et al. The efficacy of a family-based cognitive-behavioral treatment for separation anxiety disorder in children aged 8-13: a randomized comparison with a general anxiety program. J Consult Clin Psychol. 2013 Oct;81(5):932-40. doi: 10.1037/a0032678. PMID: 23607501. Exclusion Code: X4.
- 559. Schoneveld EA, Malmberg M, Lichtwarck-Aschoff A, et al. A neurofeedback video game (MindLight) to prevent anxiety in children: A randomized controlled trial. Comput Human Behav. 2016;63:321-33. doi: 10.1016/j.chb.2016.05.005. PMID: 2016-39370-036. Exclusion Code: X2.
- 560. Schopf K, Mohr C, Lippert MW, et al. The role of exposure in the treatment of anxiety in children and adolescents: protocol of a systematic review and meta-analysis. Syst Rev. 2020 Apr 27;9(1):96. doi: 10.1186/s13643-020-01337-2. PMID: 32340628. Exclusion Code: X11.
- 561. Schuppert HM, Giesen-Bloo J, van Gemert TG, et al. Effectiveness of an emotion regulation group training for adolescents--a randomized controlled pilot study. Clin Psychol Psychother. 2009 Nov-Dec;16(6):467-78. doi: 10.1002/cpp.637. PMID: 19630069. Exclusion Code: X2.
- 562. Schuppert HM, Timmerman ME, Bloo J, et al. Emotion regulation training for adolescents with borderline personality disorder traits: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2012 Dec;51(12):1314-23.e2. doi: 10.1016/j.jaac.2012.09.002. PMID: 23200288. Exclusion Code: X2.

- 563. Schwingel A, Gálvez P, Linares D, et al. Using a Mixed-Methods RE-AIM Framework to Evaluate Community Health Programs for Older Latinas. J Aging Health. 2017 Jun;29(4):551-93. doi: 10.1177/0898264316641075. PMID: 27079919. Exclusion Code: X2.
- 564. Sekhar DL, Ba DM, Liu G, et al. Major Depressive Disorder Screening Remains Low Even Among Privately Insured Adolescents. J Pediatr. 2019 Jan;204:203-7. doi: 10.1016/j.jpeds.2018.07.086. PMID: 30244990. Exclusion Code: X9.
- 565. Sekhar DL, Pattison KL, Confair A, et al. Effectiveness of Universal School-Based Screening vs Targeted Screening for Major Depressive Disorder Among Adolescents: A Trial Protocol for the Screening in High Schools to Identify, Evaluate, and Lower Depression (SHIELD) Randomized Clinical Trial. JAMA Netw Open. 2019 Nov 1;2(11):e1914427. doi: 10.1001/jamanetworkopen.2019.14427. PMID: 31675086. Exclusion Code: X5.
- 566. Seligman LD, Ollendick TH, Langley AK, et al. The utility of measures of child and adolescent anxiety: A meta-analytic review of the Revised Children's Anxiety Scale, the State-Trait Anxiety Inventory for Children, and the Child Behavior Checklist. J Clin Child Adolesc Psychol. 2004;33(3):557-65. doi: 10.1207/s15374424jccp3303_13. PMID: 2004-16801-013. Exclusion Code: X9.
- Serrani Azcurra D. Psychometric validation of the Columbia-Suicide Severity rating scale in Spanish-speaking adolescents. Colomb Med (Cali). 2017 Dec 30;48(4):174-82. doi: 10.25100/cm.v43i4.2294. PMID: 29662259. Exclusion Code: X2.
- 568. Shand FL, Ridani R, Tighe J, et al. The effectiveness of a suicide prevention app for indigenous Australian youths: study protocol for a randomized controlled trial. Trials. 2013 Nov 20;14:396. doi: 10.1186/1745-6215-14-396. PMID: 24257410. Exclusion Code: X11.
- 569. Shippee ND, Mattson A, Brennan R, et al. Effectiveness in Regular Practice of Collaborative Care for Depression Among Adolescents: A Retrospective Cohort Study. Psychiatr Serv. 2018 May 1;69(5):536-41. doi: 10.1176/appi.ps.201700298. PMID: 29446330. Exclusion Code: X7.
- 570. Shirk SR, Deprince AP, Crisostomo PS, et al. Cognitive behavioral therapy for depressed adolescents exposed to interpersonal trauma: an initial effectiveness trial. Psychotherapy (Chic). 2014 Mar;51(1):167-79. doi: 10.1037/a0034845. PMID: 24377410. Exclusion Code: X2.
- 571. Shirk SR, Gudmundsen G, Kaplinski HC, et al. Alliance and outcome in cognitive-behavioral therapy for adolescent depression. J Clin Child Adolesc Psychol. 2008 Jul;37(3):631-9. doi: 10.1080/15374410802148061. PMID: 18645753. Exclusion Code: X4.

- 572. Sigurvinsdóttir AL, Jensínudóttir KB,
 Baldvinsdóttir KD, et al. Effectiveness of
 cognitive behavioral therapy (CBT) for child and
 adolescent anxiety disorders across different CBT
 modalities and comparisons: a systematic review
 and meta-analysis. Nord J Psychiatry. 2020
 Apr;74(3):168-80. doi:
 10.1080/08039488.2019.1686653. PMID:
 31738631. Exclusion Code: X8.
- 573. Silver J, Barch DM, Klein DN, et al. A Brief Early Childhood Screening Tool for Psychopathology Risk in Primary Care: The Moderating Role of Poverty. J Pediatr. 2021 Apr 28doi: 10.1016/j.jpeds.2021.04.042. PMID: 33930406. Exclusion Code: X7.
- 574. Silverman WK, Kurtines WM, Ginsburg GS, et al. Treating anxiety disorders in children with group cognitive-behaviorial therapy: a randomized clinical trial. J Consult Clin Psychol. 1999 Dec;67(6):995-1003. doi: 10.1037//0022-006x.67.6.995. PMID: 10596522. Exclusion Code: X13.
- 575. Simeon JG, Ferguson HB. Alprazolam effects in children with anxiety disorders. Can J Psychiatry. 1987 Oct;32(7):570-4. doi: 10.1177/070674378703200712. PMID: 3315169. Exclusion Code: X3.
- 576. Simon E, Bögels SM, Voncken JM. Efficacy of child-focused and parent-focused interventions in a child anxiety prevention study. J Clin Child Adolesc Psychol. 2011;40(2):204-19. doi: 10.1080/15374416.2011.546039. PMID: 2011-05035-004. Exclusion Code: X5.
- 577. Simon E, de Hullu E, Bögels S, et al.
 Development of 'learn to dare!': An online
 assessment and intervention platform for anxious
 children. BMC Psychiatry. 2020;20PMID: 202010654-001. Exclusion Code: X11.
- 578. Simon GE, Coleman KJ, Rossom RC, et al. Risk of suicide attempt and suicide death following completion of the Patient Health Questionnaire depression module in community practice. J Clin Psychiatry. 2016 Feb;77(2):221-7. doi: 10.4088/JCP.15m09776. PMID: 26930521. Exclusion Code: X2.
- 579. Siqueland L, Rynn M, Diamond GS. Cognitive behavioral and attachment based family therapy for anxious adolescents: Phase I and II studies. J Anxiety Disord. 2005;19(4):361-81. doi: 10.1016/j.janxdis.2004.04.006. PMID: 15721570. Exclusion Code: X4.
- 580. Smith AM, Flannery-Schroeder EC, Gorman KS, et al. Parent cognitive-behavioral intervention for the treatment of childhood anxiety disorders: a pilot study. Behav Res Ther. 2014;61:156-61. doi: 10.1016/j.brat.2014.08.010. PMID: 2014-38494-001. Exclusion Code: X13.
- 581. Smith L, Jackson SE, Jacob L, et al. Leisure-Time Sedentary Behavior, Alcohol Consumption, and Sexual Intercourse Among Adolescents Aged 12-15 Years in 19 Countries From Africa, the Americas, and Asia. J Sex Med. 2019

- Sep;16(9):1355-63. doi: 10.1016/j.jsxm.2019.06.013. PMID: 31351852. Exclusion Code: X2.
- 582. Solberg JJ, Deyo-Svendsen ME, Nylander KR, et al. Collaborative Care Management Associated With Improved Depression Outcomes in Patients With Personality Disorders, Compared to Usual Primary Care. J Prim Care Community Health. 2018 Jan-Dec;9:2150132718773266. doi: 10.1177/2150132718773266. PMID: 29739287. Exclusion Code: X2.
- 583. Sood ED, Kendall PC. Assessing anxious selftalk in youth: The Negative Affectivity Self-Statement Questionnaire--Anxiety Scale. Cognit Ther Res. 2007;31(5):603-18. doi: 10.1007/s10608-006-9043-8. PMID: 2008-00189-003. Exclusion Code: X5.
- 584. Soria-Saucedo R, Walter HJ, Cabral H, et al. Receipt of Evidence-Based Pharmacotherapy and Psychotherapy Among Children and Adolescents With New Diagnoses of Depression. Psychiatr Serv. 2016 Mar;67(3):316-23. doi: 10.1176/appi.ps.201500090. PMID: 26725295. Exclusion Code: X7.
- 585. Southam-Gerow MA, Weisz JR, Chu BC, et al. Does cognitive behavioral therapy for youth anxiety outperform usual care in community clinics? An initial effectiveness test. J Am Acad Child Adolesc Psychiatry. 2010 Oct;49(10):1043-52. doi: 10.1016/j.jaac.2010.06.009. PMID: 20855049. Exclusion Code: X4.
- 586. Spence SH, Donovan C, Brechman-Toussaint M. The treatment of childhood social phobia: the effectiveness of a social skills training-based, cognitive-behavioural intervention, with and without parental involvement. J Child Psychol Psychiatry. 2000 Sep;41(6):713-26. PMID: 11039684. Exclusion Code: X13.
- 587. Spence SH, Donovan CL, March S, et al. A randomized controlled trial of online versus clinic-based CBT for adolescent anxiety. J Consult Clin Psychol. 2011 Oct;79(5):629-42. doi: 10.1037/a0024512. PMID: 21744945. Exclusion Code: X13.
- 588. Spence SH, Donovan CL, March S, et al. Generic versus disorder specific cognitive behavior therapy for social anxiety disorder in youth: a randomized controlled trial using internet delivery. Behav Res Ther. 2017 Mar;90:41-57. doi: 10.1016/j.brat.2016.12.003. PMID: 27988427. Exclusion Code: X13.
- 589. Spence SH, Holmes JM, March S, et al. The feasibility and outcome of clinic plus Internet delivery of cognitive-behavior therapy for childhood anxiety. J Consult Clin Psychol. 2006;74(3):614-21. doi: 10.1037/0022-006X.74.3.614. PMID: 2006-08433-020. Exclusion Code: X13.
- 590. Steeg S, Kapur N, Webb R, et al. The development of a population-level clinical screening tool for self-harm repetition and suicide: the ReACT Self-Harm Rule. Psychol

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- Med. 2012 Nov:42(11):2383-94. doi: 10.1017/s0033291712000347. PMID: 22394511. Exclusion Code: X3.
- 591. Sterling S, Kline-Simon AH, Weisner C, et al. Pediatrician and Behavioral Clinician-Delivered Screening, Brief Intervention and Referral to Treatment: Substance Use and Depression Outcomes. J Adolesc Health. 2018 Apr;62(4):390-6. doi: 10.1016/j.jadohealth.2017.10.016. PMID: 29396080. Exclusion Code: X9.
- 592. Stikkelbroek Y, Bodden D. Effectiveness of cognitive behaviours therapy (CBT), in clinically depressed adolescents versus Treatment As Usual (TAU). Eur Child Adolesc Psychiatry. 2015;24(1):S119-. doi: 10.1007/s00787-015-0714-4. PMID: CN-01098690. Exclusion Code:
- 593. Stikkelbroek Y, Bodden DH, Deković M, et al. Effectiveness and cost effectiveness of cognitive behavioral therapy (CBT) in clinically depressed adolescents: individual CBT versus treatment as usual (TAU). BMC Psychiatry. 2013 Nov 21;13:314. doi: 10.1186/1471-244x-13-314. PMID: 24261913. Exclusion Code: X11.
- 594. Stikkelbroek Y. Vink G. Nauta MH. et al. Effectiveness and moderators of individual cognitive behavioral therapy versus treatment as usual in clinically depressed adolescents: a randomized controlled trial. Sci Rep. 2020 Sep 9;10(1):14815. doi: 10.1038/s41598-020-71160-1. PMID: 32908173. Exclusion Code: X2.
- 595. St-Jacques J, Bouchard S, Bélanger C. Is virtual reality effective to motivate and raise interest in phobic children toward therapy? A clinical trial study of in vivo with in virtuo versus in vivo only treatment exposure. J Clin Psychiatry. 2010 Jul;71(7):924-31. doi: 10.4088/JCP.08m04822blu. PMID: 20441721. Exclusion Code: X2.
- 596. Stjerneklar S, Hougaard E, Thastum M. Guided internet-based cognitive behavioral therapy for adolescent anxiety: Predictors of treatment response. Internet Interv. 2019 Mar;15:116-25. doi: 10.1016/j.invent.2019.01.003. PMID: 30792963. Exclusion Code: X7.
- 597. Storch EA, Salloum A, King MA, et al. A randomized controlled trial in community mental health centers of computer-assisted cognitive behavioral therapy versus treatment as ususal for children with anxiety. Depress Anxiety. 2015 Nov;32(11):843-52. doi: 10.1002/da.22399. PMID: 26366886. Exclusion Code: X4.
- 598. Storch EA, Salloum A, King MA, et al. A randomized controlled trial in community mental health centers of computer-assisted cognitive behavioral therapy versus treatment as usual for children with anxiety. Depress Anxiety. 2015;32(11):843-52. doi: 10.1002/da.22399. PMID: 2015-42406-001. Exclusion Code: X10.
- 599. Strawn J, Mills J, Schroeder H, et al. Escitalopram in adolescents with generalized

- anxiety disorder: a double-blind, randomized, placebo-controlled study with pharmacogenomic and pharmacokinetic measures. Neuropsychopharmacology. 2019;44:88-9. doi: 10.1038/s41386-019-0545-y. PMID: CN-02120126. Exclusion Code: X9.
- 600. Strawn JR, Mills JA, Croarkin PE, Switching Selective Serotonin Reuptake Inhibitors in Adolescents with Selective Serotonin Reuptake Inhibitor-Resistant Major Depressive Disorder: Balancing Tolerability and Efficacy. J Child Adolesc Psychopharmacol. 2019 May;29(4):250-5. doi: 10.1089/cap.2018.0145. PMID: 30810350. Exclusion Code: X2.
- 601. Strawn JR, Mills JA, Schroeder HK, et al. 5.27 A randomized, placebo-controlled study of Escitalopram in adolescents with generalized anxiety disorder. J Am Acad Child Adolesc Psychiatry. 2019;58(10):S254-. doi: 10.1016/j.jaac.2019.08.341. PMID: CN-01999038. Exclusion Code: X10.
- 602. Strawn JR, Welge JA, Wehry AM, et al. Efficacy and tolerability of antidepressants in pediatric anxiety disorders: a systematic review and metaanalysis. Depress Anxiety. 2015 Mar;32(3):149-57. doi: 10.1002/da.22329. PMID: 25449861. Exclusion Code: X7.
- Strunk CM, King KA, Vidourek RA, et al. 603. Effectiveness of the surviving the teens® suicide prevention and depression awareness program: An impact evaluation utilizing a comparison group. Health Educ Behav. 2014;41(6):605-13. doi: 10.1177/1090198114531774. PMID: 2014-49127-005. Exclusion Code: X2.
- 604. Stulmaker HL, Ray DC. Child-centered play therapy with young children who are anxious: A controlled trial. Child Youth Serv Rev. 2015;57:127-33. doi: 10.1016/j.childyouth.2015.08.005. PMID: 2015-42972-016. Exclusion Code: X2.
- 605. Su C, Aseltine R, Doshi R, et al. Machine learning for suicide risk prediction in children and adolescents with electronic health records. Transl Psychiatry. 2020 Nov 26;10(1):413. doi: 10.1038/s41398-020-01100-0. PMID: 33243979. Exclusion Code: X3.
- 606. Sudhanthar S, Thakur K, Sigal Y, et al. Improving validated depression screen among adolescent population in primary care practice using electronic health records (EHR). BMJ Qual Improv Rep. 2015;4(1)doi: 10.1136/bmjquality.u209517.w3913. PMID: 26734415. Exclusion Code: X9.
- 607. Suveg C, Hudson JL, Brewer G, et al. Cognitivebehavioral therapy for anxiety-disordered youth: secondary outcomes from a randomized clinical trial evaluating child and family modalities. J Anxiety Disord. 2009 Apr;23(3):341-9. doi: 10.1016/j.janxdis.2009.01.003. PMID: 19216048. Exclusion Code: X4.
- 608. Swan AJ, Kendall PC, Olino T, et al. Results from the Child/Adolescent Anxiety Multimodal

516

- Longitudinal Study (CAMELS): Functional outcomes. J Consult Clin Psychol. 2018 Sep;86(9):738-50. doi: 10.1037/ccp0000334. PMID: 30138013. Exclusion Code: X7.
- 609. Swart J, Apsche J. A comparative study of mode deactivation therapy (MDT) as an effective treatment of adolescents with suicidal and non-suicidal self-injury behaviors. International Journal of Behavioral Consultation and Therapy. 2014;9(3):47-52. doi: 10.1037/h0101640. PMID: 2019-11792-010. Exclusion Code: X2.
- 610. Takagaki K, Okamoto Y, Jinnin R, et al.
 Enduring effects of a 5-week behavioral
 activation program for subthreshold depression
 among late adolescents: an exploratory
 randomized controlled trial. Neuropsychiatr Dis
 Treat. 2018;14:2633-41. doi:
 10.2147/ndt.s172385. PMID: 30349261.
 Exclusion Code: X2.
- 611. Thabrew H, Stasiak K, Bavin LM, et al.
 Validation of the Mood and Feelings
 Questionnaire (MFQ) and Short Mood and
 Feelings Questionnaire (SMFQ) in New Zealand
 help-seeking adolescents. Int J Methods Psychiatr
 Res. 2018 Sep;27(3):e1610. doi:
 10.1002/mpr.1610. PMID: 29465165. Exclusion
 Code: X2.
- 612. Thompson EA, Eggert LL, Randell BP, et al. Evaluation of indicated suicide risk prevention approaches for potential high school dropouts. Am J Public Health. 2001 May;91(5):742-52. doi: 10.2105/ajph.91.5.742. PMID: 11344882. Exclusion Code: X5.
- 613. Thompson H, Faig W, Gupta N, et al.
 Collaborative care for depression of adults and adolescents: measuring the effectiveness of screening and treatment uptake. Psychiatr Serv. 2019 Jul 1;70(7):604-7. doi: 10.1176/appi.ps.201800257. PMID: 31023189. Exclusion Code: X9.
- 614. Tighe J, Shand F, Ridani R, et al. Ibobbly mobile health intervention for suicide prevention in Australian Indigenous youth: a pilot randomised controlled trial. BMJ Open. 2017 Jan 27;7(1):e013518. doi: 10.1136/bmjopen-2016-013518. PMID: 28132007. Exclusion Code: X2.
- 615. Tillfors M, Andersson G, Ekselius L, et al. A randomized trial of internet-delivered treatment for social anxiety disorder in high school students. Cogn Behav Ther. 2011;40(2):147-57. doi: 10.1080/16506073.2011.555486. PMID: 2011-14818-007. Exclusion Code: X13.
- 616. Timbremont B, Braet C, Dreessen L. Assessing depression in youth: relation between the Children's Depression Inventory and a structured interview. J Clin Child Adolesc Psychol. 2004 Mar;33(1):149-57. doi: 10.1207/s15374424jccp3301_14. PMID: 15028549. Exclusion Code: X2.
- 617. Tompson MC, Sugar CA, Asarnow JR. Familyfocused treatment for childhood depressive disorders versus individual supportive treatment:

- results of a randomized clinical trial. J Am Acad Child Adolesc Psychiatry. 2016;55(10):S335-. doi: 10.1016/j.jaac.2016.07.403. PMID: CN-01304707. Exclusion Code: X12.
- 618. Topooco N, Berg M, Johansson S, et al. Chatand Internet-based cognitive—behavioural therapy in treatment of adolescent depression: Randomised controlled trial. BJPsych Open. 2018;4(4):199-207. doi: 10.1192/bjo.2018.18. PMID: 2019-80313-001. Exclusion Code: X10.
- 619. Topooco NW, Andersson G. Digital cognitive-behavioral therapy in the treatment of adolescent depression: a randomized controlled trial. J Am Acad Child Adolesc Psychiatry. 2017;56(10):S299-S300. doi: 10.1016/j.jaac.2017.09.411. PMID: CN-01452302. Exclusion Code: X10.
- 620. Torres Soler C, Olofsdotter S, Vadlin S, et al.
 Diagnostic accuracy of the Montgomery-Åsberg
 Depression Rating Scale parent report among
 adolescent psychiatric outpatients. Nord J
 Psychiatry. 2018 Apr;72(3):184-90. doi:
 10.1080/08039488.2017.1414873. PMID:
 29258381. Exclusion Code: X2.
- 621. Toth SL, Handley ED, Manly JT, et al. The Moderating Role of Child Maltreatment in Treatment Efficacy for Adolescent Depression. J Abnorm Child Psychol. 2020 Oct;48(10):1351-65. doi: 10.1007/s10802-020-00682-z. PMID: 32696103. Exclusion Code: X4.
- 622. Treadwell KR, Kendall PC. Self-talk in youth with anxiety disorders: states of mind, content specificity, and treatment outcome. J Consult Clin Psychol. 1996 Oct;64(5):941-50. doi: 10.1037//0022-006x.64.5.941. PMID: 8916623. Exclusion Code: X4.
- 623. Trebatická J, Hradečná Z, Böhmer F, et al. Emulsified omega-3 fatty-acids modulate the symptoms of depressive disorder in children and adolescents: a pilot study. Child Adolesc Psychiatry Ment Health. 2017;11:30. doi: 10.1186/s13034-017-0167-2. PMID: 28690672. Exclusion Code: X3.
- 624. Trentini C, Pagani M, Fania P, et al. Neural processing of emotions in traumatized children treated with Eye Movement Desensitization and Reprocessing therapy: a hdEEG study. Front Psychol. 2015;6:1662. doi: 10.3389/fpsyg.2015.01662. PMID: 26594183. Exclusion Code: X2.
- 625. Trowell J, Joffe I, Campbell J, et al. Childhood depression: a place for psychotherapy. An outcome study comparing individual psychodynamic psychotherapy and family therapy. Eur Child Adolesc Psychiatry. 2007 Apr;16(3):157-67. doi: 10.1007/s00787-006-0584-x. PMID: 17200793. Exclusion Code: X4.
- 626. Tsvieli N, Nir-Gottlieb O, Lifshitz C, et al.
 Therapist interventions associated with
 productive emotional processing in the context of
 attachment-based family therapy for depressed
 and suicidal adolescents. Fam Process.

- 2020;59(2):428-44. doi: 10.1111/famp.12445. PMID: 143653552. Language: English. Entry Date: 20200611. Revision Date: 20210601. Publication Type: Article. Exclusion Code: X7.
- 627. Tulbure BT, Andersson G, Sălăgean N, et al. Religious versus conventional internet-based cognitive behavioral therapy for depression. J Relig Health. 2018 Oct;57(5):1634-48. doi: 10.1007/s10943-017-0503-0. PMID: 29067598. Exclusion Code: X2.
- 628. Turgeon L, Chartrand E. Reliability and validity of the Revised Children's Manifest Anxiety Scale in a French-Canadian sample. Psychol Assess. 2003 Sep;15(3):378-83. doi: 10.1037/1040-3590.15.3.378. PMID: 14593838. Exclusion Code: X9.
- 629. Tze-Chun T, Shih-Yin H. Efficacy of school-based interpersonal psychotherapy to adolescents of early detected depressive and suicide ideations: randomized control study. Early intervention in psychiatry [abstracts of the 7th international conference on early psychosis early psychoses: a lifetime perspective. 29 nov 1 dec 2010; amsterdam, netherlands]. 2010PMID: CN-00851153. Exclusion Code: X5.
- 630. Valla JP, Bergeron L, Smolla N. The Dominic-R: a pictorial interview for 6- to 11-year-old children. J Am Acad Child Adolesc Psychiatry. 2000 Jan;39(1):85-93. doi: 10.1097/00004583-200001000-00020. PMID: 10638071. Exclusion Code: X7.
- of the Multidimensional Anxiety Scale for Children (MASC) for DSM-IV anxiety disorders. Depress Anxiety. 2008;25(12):1046-52. doi: 10.1002/da.20452. PMID: 18833579. Exclusion Code: X5.
- van Lang ND, Ferdinand RF, Oldehinkel AJ, et al. Concurrent validity of the DSM-IV scales Affective Problems and Anxiety Problems of the Youth Self-Report. Behav Res Ther. 2005 Nov;43(11):1485-94. doi: 10.1016/j.brat.2004.11.005. PMID: 16159590. Exclusion Code: X3.
- 633. Van Meter AR, Algorta GP, Youngstrom EA, et al. Assessing for suicidal behavior in youth using the Achenbach System of Empirically Based Assessment. Eur Child Adolesc Psychiatry. 2018 Feb;27(2):159-69. doi: 10.1007/s00787-017-1030-y. PMID: 28748484. Exclusion Code: X3.
- 634. Van Roy B, Kristensen H, Groholt B, et al. Prevalence and characteristics of significant social anxiety in children aged 8-13 years: a Norwegian cross-sectional population study. Soc Psychiatry Psychiatr Epidemiol. 2009

 May;44(5):407-15. doi: 10.1007/s00127-008-0445-7. PMID: 19015797. Exclusion Code: X7.
- 635. van Starrenburg ML, Kuijpers RC, Hutschemaekers GJ, et al. Effectiveness and underlying mechanisms of a group-based cognitive behavioural therapy-based indicative prevention program for children with elevated

- anxiety levels. BMC Psychiatry. 2013 Jul 5;13:183. doi: 10.1186/1471-244x-13-183. PMID: 23827009. Exclusion Code: X2.
- van Starrenburg ML, Kuijpers RC, Kleinjan M, et al. Effectiveness of a Cognitive Behavioral Therapy-Based Indicated Prevention Program for Children with Elevated Anxiety Levels: a Randomized Controlled Trial. Prev Sci. 2017 Jan;18(1):31-9. doi: 10.1007/s11121-016-0725-5. PMID: 27822663. Exclusion Code: X2.
- 637. Van Steensel F, Dirksen C, Bögels S. Costeffectiveness of cognitive-behavioral therapy versus treatment as usual for anxiety disorders in children with autism spectrum disorder. Res Autism Spectr Disord. 2014;8(2):127-37. Exclusion Code: X2.
- 638. Van Voorhees B, Gladstone TRG, Sobowale K, et al. 24-Month Outcomes of Primary Care Web-Based Depression Prevention Intervention in Adolescents: Randomized Clinical Trial. J Med Internet Res. 2020 Oct 28;22(10):e16802. doi: 10.2196/16802. PMID: 33112254. Exclusion Code: X2.
- 639. VanWinkle K, Kaur S, Parsh B. Screening adolescents for suicide risk. Nursing. 2020 Feb;50(2):19-20. doi: 10.1097/01.NURSE.0000615112.62845.3e. PMID: 31977801. Exclusion Code: X8.
- 640. Verhulst FC, van der Ende J, Ferdinand RF, et al. The prevalence of DSM-III-R diagnoses in a national sample of Dutch adolescents. Arch Gen Psychiatry. 1997 Apr;54(4):329-36. doi: 10.1001/archpsyc.1997.01830160049008. PMID: 9107149. Exclusion Code: X9.
- 641. Viana AG, Rabian B, Beidel DC. Self-report measures in the study of comorbidity in children and adolescents with social phobia: research and clinical utility. J Anxiety Disord. 2008
 Jun;22(5):781-92. doi:
 10.1016/j.janxdis.2007.08.005. PMID: 17888622.
 Exclusion Code: X7.
- 642. Vigerland S, Ljótsson B, Thulin U, et al. Internetdelivered cognitive behavioural therapy for children with anxiety disorders: a randomised controlled trial. Behav Res Ther. 2016;76:47-56. doi: 10.1016/j.brat.2015.11.006. PMID: 2015-59077-007. Exclusion Code: X13.
- 643. Villabø MA, Narayanan M, Compton SN, et al. Cognitive-behavioral therapy for youth anxiety: an effectiveness evaluation in community practice. J Consult Clin Psychol. 2018 Sep;86(9):751-64. doi: 10.1037/ccp0000326. PMID: 30138014. Exclusion Code: X10.
- 644. Wagner G, Zeiler M, Waldherr K, et al. Mental health problems in Austrian adolescents: a nationwide, two-stage epidemiological study applying DSM-5 criteria. Eur Child Adolesc Psychiatry. 2017 Dec;26(12):1483-99. doi: 10.1007/s00787-017-0999-6. PMID: 28540609. Exclusion Code: X9.
- 645. Wagner G, Zeiler M, Waldherr K, et al. Mental health problems in Austrian adolescents: A

518

- nationwide, two-stage epidemiological study applying DSM-5 criteria. Eur Child Adolesc Psychiatry. 2017;26(12):1483-99. doi: 10.1007/s00787-017-0999-6. PMID: 2017-23400-001. Exclusion Code: X9.
- 646. Wagner KD, Robb AS, Findling RL, et al. A randomized, placebo-controlled trial of citalopram for the treatment of major depression in children and adolescents. Am J Psychiatry. 2004 Jun;161(6):1079-83. doi: 10.1176/appi.ajp.161.6.1079. PMID: 15169696. Exclusion Code: X3.
- 647. Walkup J. The child/adolescent anxiety multimodal trial. Eur Child Adolesc Psychiatry. 2013;22(2):S165-. doi: 10.1007/s00787-013-0423-9. PMID: CN-01006225. Exclusion Code: X8
- 648. Walkup J, Labellarte M, Riddle MA, et al.
 Treatment of pediatric anxiety disorders: an
 open-label extension of the research units on
 pediatric psychopharmacology anxiety study. J
 Child Adolesc Psychopharmacol. 2002
 Fall;12(3):175-88. doi:
 10.1089/104454602760386879. PMID:
 12427292. Exclusion Code: X4.
- 649. Wang Z, Whiteside S, Sim L, et al. AHRQ comparative effectiveness reviews. Anxiety in Children. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017. Exclusion Code: X7.
- 650. Waraan L, Rognli EW, Czajkowski NO, et al. Effectiveness of attachment-based family therapy compared to treatment as usual for depressed adolescents in community mental health clinics. Child Adolesc Psychiatry Ment Health. 2021 Feb 12;15(1):8. doi: 10.1186/s13034-021-00361-x. PMID: 33579332. Exclusion Code: X4.
- 651. Waraan L, Rognli EW, Czajkowski NO, et al. Efficacy of attachment-based family therapy compared to treatment as usual for suicidal ideation in adolescents with MDD. Clin Child Psychol Psychiatry. 2021 Apr;26(2):464-74. doi: 10.1177/1359104520980776. PMID: 33349055. Exclusion Code: X4.
- 652. Warner CM, Colognori D, Kim RE, et al.
 Cognitive-behavioral treatment of persistent
 functional somatic complaints and pediatric
 anxiety: an initial controlled trial. Depress
 Anxiety. 2011 Jul;28(7):551-9. doi:
 10.1002/da.20821. PMID: 21681863. Exclusion
 Code: X13.
- 653. Waseem M, Diaz-Guerrero RJ, Cosme R, et al. Do all children with suicidal ideation receive a significant psychiatric intervention? Pediatr Int. 2015 Jun;57(3):381-4. doi: 10.1111/ped.12527. PMID: 25330120. Exclusion Code: X7.
- 654. Waters AM, Ford LA, Wharton TA, et al.

 Cognitive-behavioural therapy for young children with anxiety disorders: comparison of a child + parent condition versus a parent only condition.

 Behav Res Ther. 2009 Aug;47(8):654-62. doi:

- 10.1016/j.brat.2009.04.008. PMID: 19457471. Exclusion Code: X13.
- 655. Waters AM, Pittaway M, Mogg K, et al.
 Attention training towards positive stimuli in
 clinically anxious children. Dev Cogn Neurosci.
 2013 Apr;4:77-84. doi:
 10.1016/j.dcn.2012.09.004. PMID: 23063461.
 Exclusion Code: X4.
- 656. Waters AM, Zimmer-Gembeck MJ, Craske MG, et al. Look for good and never give up: A novel attention training treatment for childhood anxiety disorders. Behav Res Ther. 2015 Oct;73:111-23. doi: 10.1016/j.brat.2015.08.005. PMID: 26310362. Exclusion Code: X3.
- 657. Waters AM, Zimmer-Gembeck MJ, Craske MG, et al. A preliminary evaluation of a home-based, computer-delivered attention training treatment for anxious children living in regional communities. Journal of Experimental Psychopathology. 2016;7(3):511-27. doi: 10.5127/jep.053315. PMID: 2016-58566-015. Exclusion Code: X3.
- Watson DR, Garfinkel SN, Gould van Praag C, et al. Computerized Exposure Therapy for Spider Phobia: Effects of Cardiac Timing and Interoceptive Ability on Subjective and Behavioral Outcomes. Psychosom Med. 2019 Jan;81(1):90-9. doi: 10.1097/psy.00000000000000646. PMID: 30300237. Exclusion Code: X2.
- 659. Weihs KL, Murphy W, Abbas R, et al.

 Desvenlafaxine versus placebo in a fluoxetinereferenced study of children and adolescents with
 major depressive disorder. J Child Adolesc
 Psychopharmacol. 2018 Feb;28(1):36-46. doi:
 10.1089/cap.2017.0100. PMID: 29189044.
 Exclusion Code: X13.
- 660. Weisz JR, Bearman SK, Ugueto AM, et al.
 Testing Robustness of Child STEPs Effects with
 Children and Adolescents: A Randomized
 Controlled Effectiveness Trial. J Clin Child
 Adolesc Psychol. 2019 Sep 13:1-14. doi:
 10.1080/15374416.2019.1655757. PMID:
 31517543. Exclusion Code: X2.
- 661. Weitkamp K, Daniels JK, Baumeister-Duru A, et al. Effectiveness trial of psychoanalytic psychotherapy for children and adolescents with severe anxiety symptoms in a naturalistic treatment setting. British Journal of Psychotherapy. 2018;34(2):300-18. doi: 10.1111/bjp.12363. PMID: 2018-18129-012. Exclusion Code: X3.
- 662. Wergeland GJ, Fjermestad KW, Marin CE, et al. An effectiveness study of individual vs. group cognitive behavioral therapy for anxiety disorders in youth. Behav Res Ther. 2014 Jun;57:1-12. doi: 10.1016/j.brat.2014.03.007. PMID: 24727078. Exclusion Code: X13.
- 663. Whalen DJ, Gilbert KE, Luby JL. Changes in self-reported and observed parenting following a randomized control trial of parent-child interaction therapy for the treatment of preschool

519

- depression. J Child Psychol Psychiatry. 2021 Jan;62(1):86-96. doi: 10.1111/jcpp.13263. PMID: 32469454. Exclusion Code: X9.
- 664. Wharff EA, Ginnis KM, Ross AM. Family-based crisis intervention with suicidal adolescents in the emergency room: a pilot study. Soc Work. 2012 Apr;57(2):133-43. doi: 10.1093/sw/sws017. PMID: 23038875. Exclusion Code: X5.
- 665. White SW, Capriola-Hall NN, Wieckowski AT, et al. Change in gaze-based attention bias in adolescents with social anxiety disorder. Cog Emot. 2019;33(8):1736-44. doi: 10.1080/02699931.2019.1598938. PMID: 2019-18278-001. Exclusion Code: X3.
- 666. Wilkinson PO, Goodyer IM. The effects of cognitive-behavioural therapy on mood-related ruminative response style in depressed adolescents. Child Adolesc Psychiatry Ment Health. 2008 Jan 29;2(1):3. doi: 10.1186/1753-2000-2-3. PMID: 18230146. Exclusion Code: X4.
- 667. Willging CE, Green AE, Ramos MM.
 Implementing school nursing strategies to reduce LGBTQ adolescent suicide: a randomized cluster trial study protocol. Implement Sci. 2016 Oct 22;11(1):145. doi: 10.1186/s13012-016-0507-2. PMID: 27770819. Exclusion Code: X11.
- 668. Wolff JC, Garcia A, Kelly LM, et al. Feasibility of decision rule-based treatment of comorbid youth: A pilot randomized control trial. Behav Res Ther. 2020 Aug;131:103625. doi: 10.1016/j.brat.2020.103625. PMID: 32353635. Exclusion Code: X4.
- 669. Wolk CB, Jager-Hyman S, Marcus SC, et al. Developing implementation strategies for firearm safety promotion in paediatric primary care for suicide prevention in two large US health systems: a study protocol for a mixed-methods implementation study. BMJ Open. 2017 Jun 24;7(6):e014407. doi: 10.1136/bmjopen-2016-014407. PMID: 28647722. Exclusion Code: X3.
- 670. Wong DFK, Ng TK, Zhuang XY, et al.
 Cognitive-behavior therapy with and without parental involvement for anxious Chinese adolescents: A randomized controlled trial. J Fam Psychol. 2020;34(3):353-63. doi: 10.1037/fam0000585. PMID: 2019-46165-001. Exclusion Code: X2.
- 671. Wood JJ, Piacentini JC, Bergman RL, et al.
 Concurrent validity of the anxiety disorders
 section of the Anxiety Disorders Interview
 Schedule for DSM-IV: child and parent versions.
 J Clin Child Adolesc Psychol. 2002
 Sep;31(3):335-42. doi:
 10.1207/s15374424jccp3103_05. PMID:
 12149971. Exclusion Code: X2.
- 672. Wright B, Tindall L, Hargate R, et al.
 Computerised cognitive behavioural therapy for depression in adolescents: 12-month outcomes of a UK randomised controlled trial pilot study.
 Bjpsych open. 2020;6(1)doi:

- 10.1192/bjo.2019.91. PMID: CN-02205438. Exclusion Code: X2.
- 673. Wright B, Tindall L, Hargate R, et al.
 Computerised cognitive-behavioural therapy for depression in adolescents: 12-month outcomes of a UK randomised controlled trial pilot study.
 BJPsych Open. 2019 Dec 12;6(1):e5. doi: 10.1192/bjo.2019.91. PMID: 31829300.
 Exclusion Code: X2.
- 674. Wright B, Tindall L, Littlewood E, et al.
 Computerised cognitive-behavioural therapy for
 depression in adolescents: feasibility results and
 4-month outcomes of a UK randomised
 controlled trial. BMJ Open. 2017 Jan
 27;7(1):e012834. doi: 10.1136/bmjopen-2016012834. PMID: 28132000. Exclusion Code: X2.
- 675. Wright DR, Haaland WL, Ludman E, et al. The Costs and Cost-effectiveness of Collaborative Care for Adolescents With Depression in Primary Care Settings: A Randomized Clinical Trial. JAMA Pediatr. 2016 Nov 1;170(11):1048-54. doi: 10.1001/jamapediatrics.2016.1721. PMID: 27654449. Exclusion Code: X9.
- 676. Wright DR, Katon WJ, Ludman E, et al.
 Association of Adolescent Depressive Symptoms
 With Health Care Utilization and Payer-Incurred
 Expenditures. Acad Pediatr. 2016 JanFeb;16(1):82-9. doi: 10.1016/j.acap.2015.08.013.
 PMID: 26456002. Exclusion Code: X9.
- 677. Wright-Hughes A, Graham E, Farrin A, et al. Self-Harm Intervention: Family Therapy (SHIFT), a study protocol for a randomised controlled trial of family therapy versus treatment as usual for young people seen after a second or subsequent episode of self-harm. Trials. 2015 Nov 4;16:501. doi: 10.1186/s13063-015-1007-4. PMID: 26537599. Exclusion Code: X11.
- 678. Wuthrich VM, Rapee RM, Cunningham MJ, et al. A randomized controlled trial of the Cool Teens CD-ROM computerized program for adolescent anxiety. J Am Acad Child Adolesc Psychiatry. 2012 Mar;51(3):261-70. doi: 10.1016/j.jaac.2011.12.002. PMID: 22365462. Exclusion Code: X13.
- 679. Xavier A, Otero P, Blanco V, et al. Efficacy of a problem-solving intervention for the indicated prevention of suicidal risk in young Brazilians: Randomized controlled trial. Suicide Life Threat Behav. 2019 Dec;49(6):1746-61. doi: 10.1111/sltb.12568. PMID: 31237377. Exclusion Code: X6.
- 680. Yang W, Zhang JX, Ding Z, et al. Attention Bias Modification Treatment for Adolescents With Major Depression: A Randomized Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2016 Mar;55(3):208-18.e2. doi: 10.1016/j.jaac.2015.12.005. PMID: 26903254. Exclusion Code: X6.
- 681. Yang X, Stewart SM. The Beck Depression Inventory-II as a screening tool of depression in the Chinese adolescent population in Hong Kong: A validation study using the Composite

- International Diagnostic Interview as the gold standard. Asian J Psychiatr. 2020 Aug;52:102125. doi: 10.1016/j.ajp.2020.102125. PMID: 32388053. Exclusion Code: X13.
- 682. Yang Y, Dillon EC, Li M, et al. Primary care provider utilization and satisfaction with a health system navigation program for adolescents with behavioral health needs. Transl Behav Med. 2019 May 16;9(3):549-59. doi: 10.1093/tbm/ibz049. PMID: 31094446. Exclusion Code: X9.
- 683. Yap MBH, Mahtani S, Rapee RM, et al. A
 Tailored Web-Based Intervention to Improve
 Parenting Risk and Protective Factors for
 Adolescent Depression and Anxiety Problems:
 Postintervention Findings From a Randomized
 Controlled Trial. J Med Internet Res. 2018 Jan
 19;20(1):e17. doi: 10.2196/jmir.9139. PMID:
 29351895. Exclusion Code: X2.
- 684. Yee AM, Algorta GP, Youngstrom EA, et al. Unfiltered Administration of the YMRS and CDRS-R in a Clinical Sample of Children. J Clin Child Adolesc Psychol. 2015;44(6):992-1007. doi: 10.1080/15374416.2014.915548. PMID: 24885078. Exclusion Code: X2.
- 685. Yen CF, Chen YM, Cheng JW, et al. Effects of cognitive-behavioral therapy on improving anxiety symptoms, behavioral problems and parenting stress in Taiwanese children with anxiety disorders and their mothers. Child Psychiatry Hum Dev. 2014 Jun;45(3):338-47. doi: 10.1007/s10578-013-0403-9. PMID: 24002227. Exclusion Code: X4.
- 686. Yen S, Ranney ML, Krek M, et al. Skills to enhance positivity in suicidal adolescents:
 Results from a pilot randomized clinical trial. J
 Posit Psychol. 2020;15(3):348-61. doi:
 10.1080/17439760.2019.1615105. PMID:
 142382324. Language: English. Entry Date:
 20200401. Revision Date: 20200413. Publication
 Type: Article. Exclusion Code: X5.
- 687. Yen S, Spirito A, Weinstock LM, et al. Coping long term with active suicide in adolescents:

 Results from a pilot randomized controlled trial.

 Clin Child Psychol Psychiatry. 2019

- Oct;24(4):847-59. doi: 10.1177/1359104519843956. PMID: 31064203. Exclusion Code: X2.
- 688. Young J, Mufson L, Gillham JE, et al. The depression prevention initiative: effects on depression symptoms and diagnoses. Journal of the american academy of child and adolescent psychiatry. Conference: 63rd annual meeting of the american academy of child and adolescent psychiatry. United states. Conference start: 20161024. Conference end: 20161029. 2016;55(10 Supplement 1):S334-S5. doi: 10.1016/j.jaac.2016.07.402. PMID: CN-01472683. Exclusion Code: X12.
- 689. Youngstrom EA, Van Meter A, Frazier TW, et al. Developing and validating short forms of the parent general behavior inventory mania and depression scales for rating youth mood symptoms. J Clin Child Adolesc Psychol. 2020;49(2):162-77. doi: 10.1080/15374416.2018.1491006. PMID: 2018-36704-001. Exclusion Code: X2.
- 690. Zhou X, Qin B, Whittington C, et al.
 Comparative efficacy and tolerability of firstgeneration and newer-generation antidepressant
 medications for depressive disorders in children
 and adolescents: study protocol for a systematic
 review and network meta-analysis. BMJ Open.
 2015 Sep 9;5(9):e007768. doi: 10.1136/bmjopen2015-007768. PMID: 26353868. Exclusion Code:
 X11.
- 691. Zhou Y, Arend J, Mufson L, et al. Change in dysfunctional attitudes and attachment in interpersonal psychotherapy for depressed adolescents. Psychother Res. 2021 Feb;31(2):258-66. doi: 10.1080/10503307.2020.1756513. PMID: 32351173. Exclusion Code: X4.
- 692. Zwier KJ, Rao U. Buspirone use in an adolescent with social phobia and mixed personality disorder (cluster A type). J Am Acad Child Adolesc Psychiatry. 1994 Sep;33(7):1007-11. doi: 10.1097/00004583-199409000-00011. PMID: 7961339. Exclusion Code: X3.

- 1. Data Resource Center for Child & Adolescent Health. Child and Adolescent Health Measurement Initiative. 2018-2019 National Survey of Children's Health (NSCH) data query. Washington, DC: Data Resource Center for Child and Adolescent Health supported by the U.S. Department of Health and Human Services, Health Resources and Services Administration (HRSA), Maternal and Child Health Bureau (MCHB); n.d. https://www.childhealthdata.org/browse/survey/results?q=7753&r=1. Accessed May 3, 2021.
- 2. Aalsma MC, Zerr AM, Etter DJ, et al. Physician intervention to positive depression screens among adolescents in primary care. *J Adolesc Health*. 2018 Feb;62(2):212-8. doi: 10.1016/j.jadohealth.2017.08.023. PMID: 29174939.
- 3. Chowdhury T, Champion JD. Outcomes of depression screening for adolescents accessing pediatric primary care-based services. *J Pediatr Nurs*. 2020 Mar 2;52:25-9. doi: 10.1016/j.pedn.2020.02.036. PMID: 32135479.
- 4. Farley AM, Gallop RJ, Brooks ES, et al. Identification and management of adolescent depression in a large pediatric care network. *J Dev Behav Pediatr*. 2020 Feb/Mar;41(2):85-94. doi: 10.1097/dbp.000000000000750. PMID: 31651619.
- 5. Leslie KR, Chike-Harris K. Patient-administered screening tool may improve detection and diagnosis of depression among adolescents. *Clin Pediatr (Phila)*. 2018 Apr;57(4):457-60. doi: 10.1177/0009922817730343. PMID: 28950718.
- 6. Lewandowski RE, O'Connor B, Bertagnolli A, et al. Screening for and diagnosis of depression among adolescents in a large health Maintenance organization. *Psychiatr Serv.* 2016 Jun 1;67(6):636-41. doi: 10.1176/appi.ps.201400465. PMID: 26876655.
- 7. Rinke ML, German M, Azera B, et al. Effect of Mental Health Screening and Integrated Mental Health on Adolescent Depression-Coded Visits. *Clin Pediatr (Phila)*. 2019 Apr;58(4):437-45. doi: 10.1177/0009922818821889. PMID: 30623684.
- 8. Sekhar DL, Ba DM, Liu G, et al. Major Depressive Disorder Screening Remains Low Even Among Privately Insured Adolescents. *J Pediatr*. 2019 Jan;204:203-7. doi: 10.1016/j.jpeds.2018.07.086. PMID: 30244990.
- 9. Sudhanthar S, Thakur K, Sigal Y, et al. Improving validated depression screen among adolescent population in primary care practice using electronic health records (EHR). *BMJ Qual Improv Rep.* 2015;4(1)doi: 10.1136/bmjquality.u209517.w3913. PMID: 26734415.
- 10. Bose J, Zeno R, Warren B, et al. Implementation of universal adolescent depression screening: quality improvement outcomes. *J Pediatr Health Care*. 2021 Feb 10doi: 10.1016/j.pedhc.2020.08.004. PMID: 33581996.
- 11. Chavira DA, Stein MB, Bailey K, et al. Child anxiety in primary care: prevalent but untreated. *Depress Anxiety*. 2004;20(4):155-64. doi: 10.1002/da.20039. PMID: 15643639.
- 12. Etter DJ, McCord A, Ouyang F, et al. Suicide screening in primary care: use of an electronic screener to assess suicidality and improve provider follow-up for adolescents. *J Adolesc Health*. 2018 Feb;62(2):191-7. doi: 10.1016/j.jadohealth.2017.08.026. PMID: 29195764.
- Johnson JG, Harris ES, Spitzer RL, et al. The patient health questionnaire for adolescents: validation of an instrument for the assessment of mental disorders among adolescent primary care patients. *J Adolesc Health*. 2002;30(3):196-204. doi: 10.1016/S1054-139X(01)00333-0. PMID: 2002-02042-008.

- 14. O'Connor S, Ferguson E, Carney T, et al. The development and evaluation of the Paediatric Index of Emotional Distress (PI-ED). *Soc Psychiatry Psychiatr Epidemiol*. 2016 Jan;51(1):15-26. doi: 10.1007/s00127-015-1134-y. PMID: 26687238.
- 15. Christensen KS, Haugen W, Sirpal MK, et al. Diagnosis of depressed young people—criterion validity of WHO-5 and HSCL-6 in Denmark and Norway. *Fam Pract*. 2015;32(3):359-63. doi: 10.1093/fampra/cmv011. PMID: 2015-24236-019.
- 16. Roberts RE, Lewinsohn PM, Seeley JR. Screening for adolescent depression: a comparison of depression scales. *J Am Acad Child Adolesc Psychiatry*. 1991 Jan;30(1):58-66. doi: 10.1097/00004583-199101000-00009. PMID: 2005065.
- 17. Canals J, Blade J, Carbajo G, et al. The Beck Depression Inventory: psychometric characteristics and usefulness in nonclinical adolescents. *Eur J Psychol Assess*. 2001;17(1):63-8.
- 18. Garrison CZ, Addy CL, Jackson KL, et al. The CES-D as a screen for depression and other psychiatric disorders in adolescents. *J Am Acad Child Adolesc Psychiatry*. 1991 Jul;30(4):636-41. doi: 10.1097/00004583-199107000-00017. PMID: 1890099.
- 19. Patton GC, Coffey C, Posterino M, et al. A computerised screening instrument for adolescent depression: population-based validation and application to a two-phase case-control study. *Soc Psychiatry Psychiatr Epidemiol*. 1999 Mar;34(3):166-72. PMID: 10327843.
- 20. Stafford AM, Garbuz T, Etter DJ, et al. The natural course of adolescent depression treatment in the primary care setting. *J Pediatr Health Care*. 2020 Jan-Feb;34(1):38-46. doi: 10.1016/j.pedhc.2019.07.002. PMID: 31548140.
- Bailey KA, Chavira DA, Stein MT, et al. Brief measures to screen for social phobia in primary care pediatrics. *J Pediatr Psychol*. 2006 Jun;31(5):512-21. doi: 10.1093/jpepsy/jsj044. PMID: 16034004.
- 22. Chambers D, Simpson L, Hill-Briggs F, et al. Proceedings of the 8th Annual Conference on the Science of Dissemination and Implementation: Washington, DC, USA. 14-15 December 2015. *Implement Sci.* 2016 Aug 1;11 Suppl 2(Suppl 2):100. doi: 10.1186/s13012-016-0452-0. PMID: 27490260.
- 23. Queen AH, Ehrenreich-May J, Hershorin ER. Preliminary validation of a screening tool for adolescent panic disorder in pediatric primary care clinics. *Child Psychiatry Hum Dev.* 2012 Apr;43(2):171-83. doi: 10.1007/s10578-011-0256-z. PMID: 21938484.
- Thompson EA, Eggert LL. Using the suicide risk screen to identify suicidal adolescents among potential high school dropouts. *J Am Acad Child Adolesc Psychiatry*. 1999 Dec;38(12):1506-14. doi: 10.1097/00004583-199912000-00011. PMID: 10596250.
- 25. Wang Z, Whiteside S, Sim L, et al. AHRQ comparative effectiveness reviews. Anxiety in Children. Rockville (MD): Agency for Healthcare Research and Quality (US); 2017.
- Viswanathan M, Kennedy SM, McKeeman J, et al. Treatment of depression in children and adolescents: a systematic review. AHRQ Comparative Effectiveness Review Number 224. AHRQ Publication No. 20-EHC005-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2020. PMID: 32298061.
- 27. Ebrahim S, Vercammen K, Sivanand A, et al. Minimally important differences in patient or proxy-reported outcome studies relevant to children: a systematic review. *Pediatrics*. 2017 Mar;139(3):e20160833. doi: 10.1542/peds.2016-0833. PMID: 28196931.

- Jayadevappa R, Cook R, Chhatre S. Minimal important difference to infer changes in health-related quality of life-a systematic review. *J Clin Epidemiol*. 2017 Sep;89:188-98. doi: 10.1016/j.jclinepi.2017.06.009. PMID: 28676426.
- 29. Thissen D, Liu Y, Magnus B, et al. Estimating minimally important difference (MID) in PROMIS pediatric measures using the scale-judgment method. *Qual Life Res.* 2016 Jan;25(1):13-23. doi: 10.1007/s11136-015-1058-8. PMID: 26118768.
- 30. U.S. Food and Drug Administration. Suicidality in children and adolescents being treated with antidepressant medications. Silver Spring, MD: Food and Drug Administration; 2018. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/suicidality-children-and-adolescents-being-treated-antidepressant-medications. Accessed February 15, 2021.
- Ollendick TH, White SW, Richey J, et al. Attention bias modification treatment for adolescents with social anxiety disorder. *Behav Ther*. 2019 Jan;50(1):126-39. doi: 10.1016/j.beth.2018.04.002. PMID: 30661553.
- Waters AM, Zimmer-Gembeck MJ, Craske MG, et al. Look for good and never give up: A novel attention training treatment for childhood anxiety disorders. *Behav Res Ther*. 2015 Oct;73:111-23. doi: 10.1016/j.brat.2015.08.005. PMID: 26310362.
- Fitzgerald A, Rawdon C, Dooley B. A randomized controlled trial of attention bias modification training for socially anxious adolescents. *Behav Res Ther*. 2016 Sep;84:1-8. doi: 10.1016/j.brat.2016.06.003. PMID: 27379745.
- 34. Chang SW, Kuckertz JM, Bose D, et al. Efficacy of attention bias training for child anxiety disorders: a randomized controlled trial. *Child Psychiatry Hum Dev.* 2019 Apr;50(2):198-208. doi: 10.1007/s10578-018-0832-6. PMID: 30051155.
- 35. Pettit JW, Bechor M, Rey Y, et al. A Randomized Controlled Trial of Attention Bias Modification Treatment in Youth With Treatment-Resistant Anxiety Disorders. *J Am Acad Child Adolesc Psychiatry*. 2020 Jan;59(1):157-65. doi: 10.1016/j.jaac.2019.02.018. PMID: 30877049.
- 36. De Lijster JM, Dieleman GC, Utens E, et al. Online Attention Bias Modification in Combination with Cognitive-Behavioural Therapy for Children and Adolescents with Anxiety Disorders: a Randomised Controlled Trial. *Behav Change*. 2019doi: 10.1017/bec.2019.8. PMID: CN-01937771.
- 37. Bar-Haim Y, Morag I, Glickman S. Training anxious children to disengage attention from threat: A randomized controlled trial. *J Child Psychol Psychiatry*. 2011;52(8):861-9. doi: 10.1111/j.1469-7610.2011.02368.x. PMID: 2011-14641-007.
- 38. Pergamin-Hight L, Pine DS, Fox NA, et al. Attention bias modification for youth with social anxiety disorder. *J Child Psychol Psychiatry*. 2016;57(11):1317-25. doi: 10.1111/jcpp.12599. PMID: 2016-53125-007.
- Waters AM, Zimmer-Gembeck MJ, Craske MG, et al. A preliminary evaluation of a home-based, computer-delivered attention training treatment for anxious children living in regional communities. *Journal of Experimental Psychopathology*. 2016;7(3):511-27. doi: 10.5127/jep.053315. PMID: 2016-58566-015.
- 40. MacLeod C, Mathews A, Tata P. Attentional bias in emotional disorders. *J Abnorm Psychol.* 1986 Feb;95(1):15-20. doi: 10.1037//0021-843x.95.1.15. PMID: 3700842.
- Hancock KM, Swain J, Hainsworth CJ, et al. Acceptance and commitment therapy versus cognitive behavior therapy for children with anxiety: outcomes of a randomized

- controlled trial. *J Clin Child Adolesc Psychol*. 2018 Mar-Apr;47(2):296-311. doi: 10.1080/15374416.2015.1110822. PMID: 26998803.
- 42. Salzer S, Stefini A, Kronmüller KT, et al. Cognitive-behavioral and psychodynamic therapy in adolescents with social anxiety disorder: a multicenter randomized controlled trial. *Psychother Psychosom*. 2018;87(4):223-33. doi: 10.1159/000488990. PMID: 29895001.
- 43. Dietz LJ, Weinberg RJ, Brent DA, et al. Family-based interpersonal psychotherapy for depressed preadolescents: examining efficacy and potential treatment mechanisms. *J Am Acad Child Adolesc Psychiatry*. 2015 Mar;54(3):191-9. doi: 10.1016/j.jaac.2014.12.011. PMID: 25721184.
- 44. Rossello J, Bernal G. The efficacy of cognitive-behavioral and interpersonal treatments for depression in Puerto Rican adolescents. *J Consult Clin Psychol*. 1999 Oct;67(5):734-45. PMID: 10535240.
- Clarke GN, Rohde P, Lewinsohn PM, et al. Cognitive-behavioral treatment of adolescent depression: efficacy of acute group treatment and booster sessions. *J Am Acad Child Adolesc Psychiatry*. 1999 Mar;38(3):272-9. doi: 10.1097/00004583-199903000-00014. PMID: 10087688.
- 46. Tompson MC, Sugar CA, Langer DA, et al. A randomized clinical trial comparing family-focused treatment and individual supportive therapy for depression in childhood and early adolescence. *J Am Acad Child Adolesc Psychiatry*. 2017 Jun;56(6):515-23. doi: 10.1016/j.jaac.2017.03.018. PMID: 28545757.
- 47. Poole LA, Knight T, Toumbourou JW, et al. A randomized controlled trial of the impact of a family-based adolescent depression intervention on both youth and parent mental health outcomes. *J Abnorm Child Psychol*. 2018 Jan;46(1):169-81. doi: 10.1007/s10802-017-0292-7. PMID: 28374218.
- 48. Poole LA, Lewis AJ, Toumbourou JW, et al. A multi-family group intervention for adolescent depression: The BEST MOOD program. *Fam Process*. 2017;56(2):317-30. doi: 10.1111/famp.12218. PMID: 2017-25520-002.
- 49. Brent DA, Holder D, Kolko D, et al. A clinical psychotherapy trial for adolescent depression comparing cognitive, family, and supportive therapy. *Arch Gen Psychiatry*. 1997 Sep;54(9):877-85. PMID: 9294380.
- 50. O'Connor BC, Lewandowski RE, Rodriguez S, et al. Usual care for adolescent depression from symptom identification through treatment initiation. *JAMA Pediatr*. 2016 Apr;170(4):373-80. doi: 10.1001/jamapediatrics.2015.4158. PMID: 26832387.
- Thompson H, Faig W, Gupta N, et al. Collaborative care for depression of adults and adolescents: measuring the effectiveness of screening and treatment uptake. *Psychiatr Serv.* 2019 Jul 1;70(7):604-7. doi: 10.1176/appi.ps.201800257. PMID: 31023189.
- Wright DR, Katon WJ, Ludman E, et al. Association of Adolescent Depressive Symptoms With Health Care Utilization and Payer-Incurred Expenditures. *Acad Pediatr*. 2016 Jan-Feb;16(1):82-9. doi: 10.1016/j.acap.2015.08.013. PMID: 26456002.
- 53. Downey VA, Zun LS. Identifying Undiagnosed Pediatric Mental Illness in the Emergency Department. *Pediatr Emerg Care*. 2018 Feb;34(2):e21-e3. doi: 10.1097/pec.00000000001151. PMID: 28441242.
- Patel A, Watts C, Shiddell S, et al. Universal adolescent suicide screening in a pediatric urgent care center. *Arch Suicide Res.* 2018 Jan-Mar;22(1):118-27. doi: 10.1080/13811118.2017.1304303. PMID: 28281893.

- US Food and Drug Administration. Anafranil® Clomipramine Hydrochloride capsules USP (25 mg, 50 mg, and 75 mg) Silver Spring, MD: US Food and Drug Administration; 2007.
- US Food and Drug Administration. Highlights of prescribing information. Cymbalta (duloxetine hydrochloride) delayed-release capsules for oral use (reference ID: 2860327). Silver Spring, MD: US Food and Drug Administration; 2004. https://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022516lbl.pdf Accessed April 20, 2021.
- 57. U.S. Food and Drug Administration. Highlights of prescribing information. Lexapro® (escitalopram oxalate) tablets. Silver Spring, MD: U.S. Food and Drug Administration; 2017. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021323s047lbl.pdf. Accessed April 20, 2021.
- 58. U.S. Food and Drug Administration. Highlights of prescribing information. PROZAC (fluoxetine capsules) for oral use Silver Spring, MD: U.S. Food and Drug Administration; 2017.

 https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/018936s108lbl.pdf.

 Accessed April 20, 2021.
- 59. US Food and Drug Administration. Highlights of prescribing information. Luvox® (fluvoxamine maleate) Tablets for oral administration Silver Spring, MD: US Food and Drug Administration; 2008.

 https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/022235lbl.pdf. Accessed April 20, 2021.
- 60. US Food and Drug Administration. Highlights of prescribing information. ZOLOFT (sertraline hydrochloride) tablets, for oral use. Silver Spring, MD: US Food and Drug Administration; 2016.
 https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/019839S74S86S87_20990S35S44S45lbl.pdf. Accessed April 20, 2021.
- 61. US Preventive Services Task Force. Procedure Manual. US Preventive Services Task Force; 2021. https://www.uspreventiveservicestaskforce.org/uspstf/about-uspstf/methods-and-processes/procedure-manual/procedure-manual-appendix-vi-criteria-assessing-internal-validity-individual-studies Accessed August 16, 2022.
- 62. Harris RP, Helfand M, Woolf SH, et al. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001 Apr;20(3 Suppl):21-35. doi: 10.1016/s0749-3797(01)00261-6. PMID: 11306229.
- 63. Mammarella IC, Donolato E, Caviola S, et al. Anxiety profiles and protective factors: a latent profile analysis in children. *Pers Individ Dif.* 2018;124:201-8. doi: 10.1016/j.paid.2017.12.017. PMID: 2018-01016-035.
- 64. O'Connor E, Senger CA, Henninger M, et al. US Preventive Services Task Force Evidence Syntheses, formerly Systematic Evidence Reviews. Interventions to Prevent Perinatal Depression: A Systematic Evidence Review for the US Preventive Services Task Force. Agency for Healthcare Research and Quality; 2019.
- 65. Arendt K, Thastum M, Hougaard E. Efficacy of a Danish version of the Cool Kids program: a randomized wait-list controlled trial. *Acta Psychiatr Scand*. 2016;133(2):109-21. doi: 10.1111/acps.12448. PMID: 2016-00713-002.

- 66. Asarnow JR, Hughes JL, Babeva KN, et al. Cognitive-behavioral family treatment for suicide attempt prevention: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2017 Jun;56(6):506-14. doi: 10.1016/j.jaac.2017.03.015. PMID: 28545756.
- 67. Asbrand J, Heinrichs N, Schmidtendorf S, et al. Experience versus report: where are changes seen after exposure-based cognitive-behavioral therapy? A randomized controlled group treatment of childhood social anxiety disorder. *Child Psychiatry Hum Dev.* 2020 Jan 20;51(3):427-41. doi: 10.1007/s10578-019-00954-w. PMID: 31960175.
- 68. Atkinson SD, Prakash A, Zhang Q, et al. A double-blind efficacy and safety study of duloxetine flexible dosing in children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol*. 2014 May;24(4):180-9. doi: 10.1089/cap.2013.0146. PMID: 24813026.
- 69. Baer S, Garland EJ. Pilot study of community-based cognitive behavioral group therapy for adolescents with social phobia. *J Am Acad Child Adolesc Psychiatry*. 2005 Mar;44(3):258-64. doi: 10.1097/00004583-200503000-00010. PMID: 15725970.
- 70. Barrett PM, Dadds MR, Rapee RM. Family treatment of childhood anxiety: a controlled trial. *J Consult Clin Psychol*. 1996 Apr;64(2):333-42. doi: 10.1037//0022-006x.64.2.333. PMID: 8871418.
- 71. Barrett PM. Evaluation of cognitive-behavioral group treatments for childhood anxiety disorders. *J Clin Child Psychol*. 1998 Dec;27(4):459-68. doi: 10.1207/s15374424jccp2704 10. PMID: 9866083.
- 72. Beidel DC, Turner SM, Sallee FR, et al. SET-C versus fluoxetine in the treatment of childhood social phobia. *J Am Acad Child Adolesc Psychiatry*. 2007;46(12):1622-32. doi: 10.1097/chi.0b013e318154bb57. PMID: 2007-18374-011.
- 73. Birmaher B, Axelson DA, Monk K, et al. Fluoxetine for the treatment of childhood anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2003 Apr;42(4):415-23. doi: 10.1097/01.Chi.0000037049.04952.9f. PMID: 12649628.
- 74. Black B, Uhde TW. Treatment of elective mutism with fluoxetine: a double-blind, placebo-controlled study. *J Am Acad Child Adolesc Psychiatry*. 1994 Sep;33(7):1000-6. doi: 10.1097/00004583-199409000-00010. PMID: 7961338.
- 75. Clarke G, DeBar LL, Pearson JA, et al. Cognitive behavioral therapy in primary care for youth declining antidepressants: a randomized trial. *Pediatrics*. 2016 May;137(5):e20151851. doi: 10.1542/peds.2015-1851. PMID: 27244782.
- 76. Clarke G, Debar L, Lynch F, et al. A randomized effectiveness trial of brief cognitive-behavioral therapy for depressed adolescents receiving antidepressant medication. *J Am Acad Child Adolesc Psychiatry*. 2005 Sep;44(9):888-98. PMID: 16113617.
- 77. Cobham VE, Filus A, Sanders MR. Working with parents to treat anxiety-disordered children: a proof of concept RCT evaluating Fear-less Triple P. *Behav Res Ther*. 2017 Aug;95:128-38. doi: 10.1016/j.brat.2017.06.004. PMID: 28641122.
- 78. Cobham VE. Do anxiety-disordered children need to come into the clinic for efficacious treatment? *J Consult Clin Psychol*. 2012;80(3):465-76. doi: 10.1037/a0028205. PMID: 2012-10793-001.
- 79. Cornacchio D, Furr JM, Sanchez AL, et al. Intensive group behavioral treatment (IGBT) for children with selective mutism: a preliminary randomized clinical trial. *J Consult Clin Psychol*. 2019 Aug;87(8):720-33. doi: 10.1037/ccp0000422. PMID: 31294589.
- 80. Cottrell DJ, Wright-Hughes A, Collinson M, et al. Effectiveness of systemic family therapy versus treatment as usual for young people after self-harm: a pragmatic, phase 3,

- multicentre, randomised controlled trial. *Lancet Psychiatry*. 2018 Mar;5(3):203-16. doi: 10.1016/s2215-0366(18)30058-0. PMID: 29449180.
- Diamond GS, Reis BF, Diamond GM, et al. Attachment-based family therapy for depressed adolescents: a treatment development study. *J Am Acad Child Adolesc Psychiatry*. 2002 Oct;41(10):1190-6. doi: 10.1097/00004583-200210000-00008. PMID: 12364840.
- 82. Diamond GS, Wintersteen MB, Brown GK, et al. Attachment-based family therapy for adolescents with suicidal ideation: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2010 Feb;49(2):122-31. doi: 10.1097/00004583-201002000-00006. PMID: 20215934.
- 83. Donovan CL, March S. Online CBT for preschool anxiety disorders: a randomised control trial. *Behav Res Ther*. 2014 Jul;58:24-35. doi: 10.1016/j.brat.2014.05.001. PMID: 24927471.
- 84. Ehrenreich-May J, Rosenfield D, Queen AH, et al. An initial waitlist-controlled trial of the unified protocol for the treatment of emotional disorders in adolescents. *J Anxiety Disord*. 2017 Mar;46:46-55. doi: 10.1016/j.janxdis.2016.10.006. PMID: 27771133.
- 85. Emslie GJ, Prakash A, Zhang Q, et al. A double-blind efficacy and safety study of duloxetine fixed doses in children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol*. 2014 May;24(4):170-9. doi: 10.1089/cap.2013.0096. PMID: 24815533.
- 86. Emslie GJ, Ventura D, Korotzer A, et al. Escitalopram in the treatment of adolescent depression: a randomized placebo-controlled multisite trial. *J Am Acad Child Adolesc Psychiatry*. 2009 Jul;48(7):721-9. doi: 10.1097/CHI.0b013e3181a2b304. PMID: 19465881.
- 87. Emslie GJ, Heiligenstein JH, Wagner KD, et al. Fluoxetine for acute treatment of depression in children and adolescents: a placebo-controlled, randomized clinical trial. *J Am Acad Child Adolesc Psychiatry*. 2002 Oct;41(10):1205-15. doi: 10.1097/00004583-200210000-00010. PMID: 12364842.
- 88. Emslie GJ, Rush AJ, Weinberg WA, et al. A double-blind, randomized, placebocontrolled trial of fluoxetine in children and adolescents with depression. *Arch Gen Psychiatry*. 1997 Nov;54(11):1031-7. PMID: 9366660.
- 89. Flannery-Schroeder EC, Kendall PC. Group and individual cognitive-behavioral treatments for youth with anxiety disorders: A randomized clinical trial. *Cognit Ther Res.* 2000;24(3):251-78.
- 90. Fristad MA, Vesco AT, Young AS, et al. Pilot randomized controlled trial of omega-3 and individual-family psychoeducational psychotherapy for children and adolescents with depression. *J Clin Child Adolesc Psychol*. 2019;48(sup1):S105-s18. doi: 10.1080/15374416.2016.1233500. PMID: 27819485.
- 91. Gallagher HM, Rabian BA, McCloskey MS. A brief group cognitive-behavioral intervention for social phobia in childhood. *J Anxiety Disord*. 2004;18(4):459-79. doi: 10.1016/S0887-6185(03)00027-6. PMID: 2004-14970-002.
- 92. Ginsburg GS, Pella JE, Pikulski PJ, et al. School-Based Treatment for Anxiety Research Study (STARS): a randomized controlled effectiveness trial. *J Abnorm Child Psychol*. 2020 Mar;48(3):407-17. doi: 10.1007/s10802-019-00596-5. PMID: 31749064.

- 93. Green JM, Wood AJ, Kerfoot MJ, et al. Group therapy for adolescents with repeated self harm: randomised controlled trial with economic evaluation. *BMJ*. 2011 Apr 1;342:d682. doi: 10.1136/bmj.d682. PMID: 21459975.
- 94. Griffiths H, Duffy F, Duffy L, et al. Efficacy of mentalization-based group therapy for adolescents: the results of a pilot randomised controlled trial. *BMC Psychiatry*. 2019 Jun 6;19(1):167. doi: 10.1186/s12888-019-2158-8. PMID: 31170947.
- 95. Hazell PL, Martin G, McGill K, et al. Group therapy for repeated deliberate self-harm in adolescents: failure of replication of a randomized trial. *J Am Acad Child Adolesc Psychiatry*. 2009 Jun;48(6):662-70. doi: 10.1097/CHI.0b013e3181aOacec. PMID: 19454922.
- 96. Hetrick SE, Yuen HP, Bailey E, et al. Internet-based cognitive behavioural therapy for young people with suicide-related behaviour (Reframe-IT): a randomised controlled trial. *Evid Based Ment Health*. 2017 Aug;20(3):76-82. doi: 10.1136/eb-2017-102719. PMID: 28701336.
- 97. Hill RM, Pettit JW. Pilot randomized controlled trial of LEAP: a selective preventive intervention to reduce adolescents' perceived burdensomeness. *J Clin Child Adolesc Psychol*. 2019;48:S45-S56. doi: 10.1080/15374416.2016.1188705. PMID: CN-01916512.
- 98. Hirshfeld-Becker DR, Masek B, Henin A, et al. Cognitive behavioral therapy for 4- to 7-year-old children with anxiety disorders: a randomized clinical trial. *J Consult Clin Psychol*. 2010 Aug;78(4):498-510. doi: 10.1037/a0019055. PMID: 20658807.
- 99. Holmes MC, Donovan CL, Farrell LJ, et al. The efficacy of a group-based, disorder-specific treatment program for childhood GAD—a randomized controlled trial. *Behav Res Ther.* 2014 Oct;61:122-35. doi: 10.1016/j.brat.2014.08.002. PMID: 25193003.
- 100. Hooven C, Walsh E, Pike KC, et al. Promoting CARE: including parents in youth suicide prevention. *Fam Community Health*. 2012 Jul-Sep;35(3):225-35. doi: 10.1097/FCH.0b013e318250bcf9. PMID: 22617413.
- 101. Infantino A, Donovan CL, March S. A randomized controlled trial of an audio-based treatment program for child anxiety disorders. *Behav Res Ther*. 2016 Apr;79:35-45. doi: 10.1016/j.brat.2016.02.007. PMID: 26950257.
- Ingul JM, Aune T, Nordahl HM. A randomized controlled trial of individual cognitive therapy, group cognitive behaviour therapy and attentional placebo adolescent social phobia. *Psychother Psychosom*. 2014;83(1):54-61. doi: 10.1159/000354672. PMID: 2013-41405-007.
- Ishikawa SI, Kikuta K, Sakai M, et al. A randomized controlled trial of a bidirectional cultural adaptation of cognitive behavior therapy for children and adolescents with anxiety disorders. *Behav Res Ther*. 2019 Sep;120:103432. doi: 10.1016/j.brat.2019.103432. PMID: 31299461.
- 104. Kendall PC, Flannery-Schroeder E, Panichelli-Mindel SM, et al. Therapy for youths with anxiety disorders: a second randomized clinical trial. *J Consult Clin Psychol*. 1997 Jun;65(3):366-80. doi: 10.1037//0022-006x.65.3.366. PMID: 9170760.
- 105. Kendall PC. Treating anxiety disorders in children: results of a randomized clinical trial. *J Consult Clin Psychol*. 1994;62(1):100.
- 106. Khanna MS, Kendall PC. Computer-assisted cognitive behavioral therapy for child anxiety: results of a randomized clinical trial. *J Consult Clin Psychol*. 2010;78(5):737-45. doi: 10.1037/a0019739. PMID: 2010-19874-014.

- 107. King CA, Gipson PY, Horwitz AG, et al. Teen options for change: an intervention for young emergency patients who screen positive for suicide risk. *Psychiatr Serv.* 2015 Jan 1;66(1):97-100. doi: 10.1176/appi.ps.201300347. PMID: 25321886.
- 108. King CA, Klaus N, Kramer A, et al. The Youth-Nominated Support Team-Version II for suicidal adolescents: a randomized controlled intervention trial. *J Consult Clin Psychol*. 2009 Oct;77(5):880-93. doi: 10.1037/a0016552. PMID: 19803568.
- Last CG, Hansen C, Franco N. Cognitive-behavioral treatment of school phobia. *J Am Acad Child Adolesc Psychiatry*. 1998 Apr;37(4):404-11. doi: 10.1097/00004583-199804000-00018. PMID: 9549961.
- Lau W-y, Chan CK-y, Li JC-h, et al. Effectiveness of group cognitive-behavioral treatment for childhood anxiety in community clinics. *Behav Res Ther*. 2010;48(11):1067-77. doi: 10.1016/j.brat.2010.07.007. PMID: 2010-16900-001.
- 111. Luby JL, Barch DM, Whalen D, et al. A randomized controlled trial of parent-child psychotherapy targeting emotion development for early childhood depression. *Am J Psychiatry*. 2018 Nov 1;175(11):1102-10. doi: 10.1176/appi.ajp.2018.18030321. PMID: 29921144.
- Lyneham HJ, Rapee RM. Evaluation of therapist-supported parent-implemented CBT for anxiety disorders in rural children. *Behav Res Ther*. 2006;44(9):1287-300. doi: 10.1016/j.brat.2005.09.009. PMID: 2006-09968-007.
- March J, Silva S, Petrycki S, et al. Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS) randomized controlled trial. *JAMA*. 2004 Aug 18;292(7):807-20. doi: 10.1001/jama.292.7.807. PMID: 15315995.
- March S, Spence SH, Donovan CL. The efficacy of an internet-based cognitive-behavioral therapy intervention for child anxiety disorders. *J Pediatr Psychol*. 2009 Jun;34(5):474-87. doi: 10.1093/jpepsy/jsn099. PMID: 18794187.
- 115. Mehlum L, Tørmoen AJ, Ramberg M, et al. Dialectical behavior therapy for adolescents with repeated suicidal and self-harming behavior: a randomized trial. *J Am Acad Child Adolesc Psychiatry*. 2014 Oct;53(10):1082-91. doi: 10.1016/j.jaac.2014.07.003. PMID: 25245352.
- Melfsen S, Kühnemund M, Schwieger J, et al. Cognitive behavioral therapy of socially phobic children focusing on cognition: a randomised wait-list control study. *Child Adolesc Psychiatry Ment Health*. 2011 Feb 28;5(1):5. doi: 10.1186/1753-2000-5-5. PMID: 21356037.
- 117. Mufson L, Weissman MM, Moreau D, et al. Efficacy of interpersonal psychotherapy for depressed adolescents. *Arch Gen Psychiatry*. 1999 Jun;56(6):573-9. PMID: 10359475.
- Mufson L, Dorta KP, Wickramaratne P, et al. A randomized effectiveness trial of interpersonal psychotherapy for depressed adolescents. *Arch Gen Psychiatry*. 2004 Jun;61(6):577-84. doi: 10.1001/archpsyc.61.6.577. PMID: 15184237.
- Nauta MH, Scholing A, Emmelkamp PM, et al. Cognitive-behavioral therapy for children with anxiety disorders in a clinical setting: no additional effect of a cognitive parent training. *J Am Acad Child Adolesc Psychiatry*. 2003 Nov;42(11):1270-8. doi: 10.1097/01.chi.0000085752.71002.93. PMID: 14566163.
- Öst L-G, Cederlund R, Reuterskiöld L. Behavioral treatment of social phobia in youth: does parent education training improve the outcome? *Behav Res Ther*. 2015;67:19-29. doi: 10.1016/j.brat.2015.02.001. PMID: 2015-12473-003.

- Ougrin D, Boege I, Stahl D, et al. Randomised controlled trial of therapeutic assessment versus usual assessment in adolescents with self-harm: 2-year follow-up. *Arch Dis Child*. 2013 Oct;98(10):772-6. doi: 10.1136/archdischild-2012-303200. PMID: 23709314.
- 122. Perrin S, Bevan D, Payne S, et al. GAD-specific cognitive behavioral treatment for children and adolescents: a pilot randomized controlled trial. *Cognit Ther Res*. 2019;43:1051-64. doi: 10.1007/s10608-019-10020-3. PMID: CN-01941262.
- Pincus DB, May JE, Whitton SW, et al. Cognitive-behavioral treatment of panic disorder in adolescence. *J Clin Child Adolesc Psychol*. 2010;39(5):638-49. doi: 10.1080/15374416.2010.501288. PMID: 2010-17041-004.
- 124. Pine DS, Walkup JT, Labellarte MJ, et al. Fluvoxamine for the treatment of anxiety disorders in children and adolescents. *N Engl J Med*. 2001;344(17):1279-85. doi: 10.1056/NEJM200104263441703. PMID: CN-00343009.
- Pineda J, Dadds MR. Family intervention for adolescents with suicidal behavior: a randomized controlled trial and mediation analysis. *J Am Acad Child Adolesc Psychiatry*. 2013 Aug;52(8):851-62. doi: 10.1016/j.jaac.2013.05.015. PMID: 23880495.
- Rapee RM, Abbott MJ, Lyneham HJ. Bibliotherapy for children with anxiety disorders using written materials for parents: a randomized controlled trial. *J Consult Clin Psychol*. 2006 Jun;74(3):436-44. doi: 10.1037/0022-006x.74.3.436. PMID: 16822101.
- 127. Richardson LP, Ludman E, McCauley E, et al. Collaborative care for adolescents with depression in primary care: a randomized clinical trial. *JAMA*. 2014 Aug 27;312(8):809-16. doi: 10.1001/jama.2014.9259. PMID: 25157724.
- 128. Rossouw TI, Fonagy P. Mentalization-based treatment for self-harm in adolescents: a randomized controlled trial. *J Am Acad Child Adolesc Psychiatry*. 2012 Dec;51(12):1304-13.e3. doi: 10.1016/j.jaac.2012.09.018. PMID: 23200287.
- Rudy BM, Zavrou S, Johnco C, et al. Parent-led exposure therapy: a pilot study of a brief behavioral treatment for anxiety in young children. *J Child Fam Stud*. 2017;26(9):2475-84. doi: 10.1007/s10826-017-0772-y. PMID: 2017-22955-001.
- 130. Rynn MA, Siqueland L, Rickels K. Placebo-controlled trial of sertraline in the treatment of children with generalized anxiety disorder. *Am J Psychiatry*. 2001 Dec;158(12):2008-14. doi: 10.1176/appi.ajp.158.12.2008. PMID: 11729017.
- 131. Sánchez-García R, Olivares Rodríguez J. Effectiveness of a program for early detection/intervention in children/adolescents with generalized social phobia. *Anales de Psicología*. 2009;25(2).
- 132. Santucci LC, Ehrenreich-May J. A randomized controlled trial of the child anxiety multi-day program (CAMP) for separation anxiety disorder. *Child Psychiatry Hum Dev.* 2013 Jun;44(3):439-51. doi: 10.1007/s10578-012-0338-6. PMID: 23053618.
- 133. Schneider S, Blatter-Meunier J, Herren C, et al. Disorder-specific cognitive-behavioral therapy for separation anxiety disorder in young children: a randomized waiting-list-controlled trial. *Psychother Psychosom*. 2011;80(4):206-15. doi: 10.1159/000323444. PMID: 2011-23503-003.
- 134. Shortt AL, Barrett PM, Fox TL. Evaluating the FRIENDS program: a cognitive-behavioral group treatment for anxious children and their parents. *J Clin Child Psychol*. 2001 Dec;30(4):525-35. doi: 10.1207/s15374424jccp3004_09. PMID: 11708240.
- 135. Silverman WK, Kurtines WM, Ginsburg GS, et al. Treating anxiety disorders in children with group cognitive-behaviorial therapy: a randomized clinical trial. *J Consult Clin*

- Psychol. 1999 Dec;67(6):995-1003. doi: 10.1037//0022-006x.67.6.995. PMID: 10596522.
- 136. Smith AM, Flannery-Schroeder EC, Gorman KS, et al. Parent cognitive-behavioral intervention for the treatment of childhood anxiety disorders: a pilot study. *Behav Res Ther*. 2014;61:156-61. doi: 10.1016/j.brat.2014.08.010. PMID: 2014-38494-001.
- 137. Spence SH, Donovan CL, March S, et al. Generic versus disorder specific cognitive behavior therapy for social anxiety disorder in youth: a randomized controlled trial using internet delivery. *Behav Res Ther*. 2017 Mar;90:41-57. doi: 10.1016/j.brat.2016.12.003. PMID: 27988427.
- 138. Spence SH, Holmes JM, March S, et al. The feasibility and outcome of clinic plus Internet delivery of cognitive-behavior therapy for childhood anxiety. *J Consult Clin Psychol*. 2006;74(3):614-21. doi: 10.1037/0022-006X.74.3.614. PMID: 2006-08433-020.
- 139. Spence SH, Donovan C, Brechman-Toussaint M. The treatment of childhood social phobia: the effectiveness of a social skills training-based, cognitive-behavioural intervention, with and without parental involvement. *J Child Psychol Psychiatry*. 2000 Sep;41(6):713-26. PMID: 11039684.
- 140. Spence SH, Donovan CL, March S, et al. A randomized controlled trial of online versus clinic-based CBT for adolescent anxiety. *J Consult Clin Psychol*. 2011 Oct;79(5):629-42. doi: 10.1037/a0024512. PMID: 21744945.
- 141. Stjerneklar S, Hougaard E, McLellan LF, et al. A randomized controlled trial examining the efficacy of an internet-based cognitive behavioral therapy program for adolescents with anxiety disorders. *PLoS One*. 2019;14(9):e0222485. doi: 10.1371/journal.pone.0222485. PMID: 31532802.
- 142. Strawn JR, Prakash A, Zhang Q, et al. A randomized, placebo-controlled study of duloxetine for the treatment of children and adolescents with generalized anxiety disorder. *J Am Acad Child Adolesc Psychiatry*. 2015 Apr;54(4):283-93. doi: 10.1016/j.jaac.2015.01.008. PMID: 25791145.
- 143. Strawn JR, Mills JA, Schroeder H, et al. Escitalopram in adolescents with generalized anxiety disorder: a double-blind, randomized, placebo-controlled study. *J Clin Psychiatry*. 2020 Aug 25;81(5):20m13396. doi: 10.4088/JCP.20m13396. PMID: 32857933.
- Tang TC, Jou SH, Ko CH, et al. Randomized study of school-based intensive interpersonal psychotherapy for depressed adolescents with suicidal risk and parasuicide behaviors. *Psychiatry Clin Neurosci*. 2009 Aug;63(4):463-70. doi: 10.1111/j.1440-1819.2009.01991.x. PMID: 19531111.
- Thirlwall K, Cooper PJ, Karalus J, et al. Treatment of child anxiety disorders via guided parent-delivered cognitive-behavioural therapy: randomised controlled trial. *Br J Psychiatry*. 2013;203(6):436-44. doi: 10.1192/bjp.bp.113.126698. PMID: CN-00910881.
- Tillfors M, Andersson G, Ekselius L, et al. A randomized trial of internet-delivered treatment for social anxiety disorder in high school students. *Cogn Behav Ther*. 2011;40(2):147-57. doi: 10.1080/16506073.2011.555486. PMID: 2011-14818-007.
- Topooco N, Berg M, Johansson S, et al. Chat- and internet-based cognitive-behavioural therapy in treatment of adolescent depression: randomised controlled trial. *BJPsych Open*. 2018 Jul;4(4):199-207. doi: 10.1192/bjo.2018.18. PMID: 29988969.
- 148. Topooco N, Byléhn S, Dahlström Nysäter E, et al. Evaluating the efficacy of internetdelivered cognitive behavioral therapy blended with synchronous chat sessions to treat

- adolescent depression: randomized controlled trial. *J Med Internet Res.* 2019 Nov 1;21(11):e13393. doi: 10.2196/13393. PMID: 31682572.
- 149. Vigerland S, Ljótsson B, Thulin U, et al. Internet-delivered cognitive behavioural therapy for children with anxiety disorders: a randomised controlled trial. *Behav Res Ther*. 2016;76:47-56. doi: 10.1016/j.brat.2015.11.006. PMID: 2015-59077-007.
- Villabø MA, Narayanan M, Compton SN, et al. Cognitive—behavioral therapy for youth anxiety: an effectiveness evaluation in community practice. *J Consult Clin Psychol*. 2018;86(9):751-64. doi: 10.1037/ccp0000326. PMID: 2018-41322-004.
- 151. Wagner KD, Jonas J, Findling RL, et al. A double-blind, randomized, placebo-controlled trial of escitalopram in the treatment of pediatric depression. *J Am Acad Child Adolesc Psychiatry*. 2006 Mar;45(3):280-8. doi: 10.1097/01.chi.0000192250.38400.9e. PMID: 16540812.
- Waite P, Marshall T, Creswell C. A randomized controlled trial of internet-delivered cognitive behaviour therapy for adolescent anxiety disorders in a routine clinical care setting with and without parent sessions. *Child Adolesc Ment Health*. 2019;24(3):242-50. doi: 10.1111/camh.12311. PMID: CN-01917999.
- Walkup JT, Albano AM, Piacentini J, et al. Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. *N Engl J Med*. 2008 Dec 25;359(26):2753-66. doi: 10.1056/NEJMoa0804633. PMID: 18974308.
- Warner CM, Colognori D, Kim RE, et al. Cognitive-behavioral treatment of persistent functional somatic complaints and pediatric anxiety: an initial controlled trial. *Depress Anxiety*. 2011 Jul;28(7):551-9. doi: 10.1002/da.20821. PMID: 21681863.
- Waters AM, Ford LA, Wharton TA, et al. Cognitive-behavioural therapy for young children with anxiety disorders: comparison of a child + parent condition versus a parent only condition. *Behav Res Ther*. 2009 Aug;47(8):654-62. doi: 10.1016/j.brat.2009.04.008. PMID: 19457471.
- Weersing VR, Brent DA, Rozenman MS, et al. Brief behavioral therapy for pediatric anxiety and depression in primary care: a randomized clinical trial. *JAMA Psychiatry*. 2017 Jun 1;74(6):571-8. doi: 10.1001/jamapsychiatry.2017.0429. PMID: 28423145.
- Weihs KL, Murphy W, Abbas R, et al. Desvenlafaxine versus placebo in a fluoxetine-referenced study of children and adolescents with major depressive disorder. *J Child Adolesc Psychopharmacol*. 2018 Feb;28(1):36-46. doi: 10.1089/cap.2017.0100. PMID: 29189044.
- Wergeland GJ, Fjermestad KW, Marin CE, et al. An effectiveness study of individual vs. group cognitive behavioral therapy for anxiety disorders in youth. *Behav Res Ther*. 2014 Jun;57:1-12. doi: 10.1016/j.brat.2014.03.007. PMID: 24727078.
- 159. Wood A, Trainor G, Rothwell J, et al. Randomized trial of group therapy for repeated deliberate self-harm in adolescents. *J Am Acad Child Adolesc Psychiatry*. 2001 Nov;40(11):1246-53. doi: 10.1097/00004583-200111000-00003. PMID: 11699797.
- Wuthrich VM, Rapee RM, Cunningham MJ, et al. A randomized controlled trial of the Cool Teens CD-ROM computerized program for adolescent anxiety. *J Am Acad Child Adolesc Psychiatry*. 2012 Mar;51(3):261-70. doi: 10.1016/j.jaac.2011.12.002. PMID: 22365462.
- 161. Cipriani A, Zhou X, Del Giovane C, et al. Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: a network

- meta-analysis. *Lancet*. 2016 Aug 27;388(10047):881-90. doi: 10.1016/s0140-6736(16)30385-3. PMID: 27289172.
- 162. Canals J, Hernández-Martínez C, Cosi S, et al. Examination of a cutoff score for the Screen for Child Anxiety Related Emotional Disorders (SCARED) in a non-clinical Spanish population. *J Anxiety Disord*. 2012 Dec;26(8):785-91. doi: 10.1016/j.janxdis.2012.07.008. PMID: 23023158.
- 163. Cunha M, Gouveia JP, do Céu Salvador M. Social fears in adolescence: the social anxiety and avoidance scale for adolescents. *Eur Psychol*. 2008;13(3):197-213. doi: 10.1027/1016-9040.13.3.197. PMID: 2008-13222-006.
- 164. Garcia-Lopez LJ, Sáez-Castillo AJ, Beidel D, et al. Brief measures to screen for social anxiety in adolescents. *J Dev Behav Pediatr*. 2015 Oct;36(8):562-8. doi: 10.1097/dbp.000000000000213. PMID: 26349070.
- 165. Gardner W, Lucas A, Kolko DJ, et al. Comparison of the PSC-17 and alternative mental health screens in an at-risk primary care sample. *J Am Acad Child Adolesc Psychiatry*. 2007 May;46(5):611-8. doi: 10.1097/chi.0b013e318032384b. PMID: 17450052.
- 166. Hopper SM, Woo JW, Sharwood LN, et al. Prevalence of suicidality in asymptomatic adolescents in the paediatric emergency department and utility of a screening tool. *Emerg Med Australas*. 2012 Oct;24(5):540-6. doi: 10.1111/j.1742-6723.2012.01576.x. PMID: 23039296.
- Johnson HS, Inderbitzen-Nolan HM, Anderson ER. The social phobia inventory: validity and reliability in an adolescent community sample. *Psychol Assess*. 2006 Sep;18(3):269-77. doi: 10.1037/1040-3590.18.3.269. PMID: 16953730.
- 168. Katon W, Russo J, Richardson L, et al. Anxiety and depression screening for youth in a primary care population. *Ambul Pediatr*. 2008 May-Jun;8(3):182-8. doi: 10.1016/j.ambp.2008.01.003. PMID: 18501865.
- Muris P, Merckelbach H, Kindt M, et al. The utility of Screen for Child Anxiety Related Emotional Disorders (SCARED) as a tool for identifying children at high risk for prevalent anxiety disorders. *Anxiety Stress Coping*. 2001;14(3):265-83. doi: 10.1080/10615800108248357. PMID: 2002-00834-002.
- 170. Ranta K, Kaltiala-Heino R, Rantanen P, et al. Screening social phobia in adolescents from general population: the validity of the Social Phobia Inventory (SPIN) against a clinical interview. *Eur Psychiatry*. 2007 May;22(4):244-51. doi: 10.1016/j.eurpsy.2006.12.002. PMID: 17346941.
- 171. Ranta K, Kaltiala-Heino R, Rantanen P, et al. The Mini-Social Phobia Inventory: psychometric properties in an adolescent general population sample. *Compr Psychiatry*. 2012 Jul;53(5):630-7. doi: 10.1016/j.comppsych.2011.07.007. PMID: 21944882.
- 172. Rivera-Riquelme M, Piqueras JA, Cuijpers P. The Revised Mental Health Inventory-5 (MHI-5) as an ultra-brief screening measure of bidimensional mental health in children and adolescents. *Psychiatry Res.* 2019 Apr;274:247-53. doi: 10.1016/j.psychres.2019.02.045. PMID: 30818147.
- Tsai CF, Wang SJ, Juang KD, et al. Use of the Chinese (Taiwan) version of the Social Phobia Inventory (SPIN) among early adolescents in rural areas: reliability and validity study. *J Chin Med Assoc*. 2009 Aug;72(8):422-9. doi: 10.1016/s1726-4901(09)70399-5. PMID: 19686998.

- 174. Stein MB, Roy-Byrne PP, McQuaid JR, et al. Development of a brief diagnostic screen for panic disorder in primary care. *Psychosom Med.* 1999 May-Jun;61(3):359-64. doi: 10.1097/00006842-199905000-00016. PMID: 10367617.
- 175. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961 Jun;4:561-71. doi: 10.1001/archpsyc.1961.01710120031004. PMID: 13688369.
- Olsson G, von Knorring AL. Depression among Swedish adolescents measured by the self-rating scale Center for Epidemiology Studies-Depression Child (CES-DC). *Eur Child Adolesc Psychiatry*. 1997 Jun;6(2):81-7. PMID: 9257089.
- 177. Fendrich M, Weissman MM, Warner V. Screening for depressive disorder in children and adolescents: validating the Center for Epidemiologic Studies Depression Scale for Children. *Am J Epidemiol*. 1990 Mar;131(3):538-51. PMID: 2301363.
- 178. Radloff LS. The CES-D scale: a self report depression scale for research in the general population. *App Psychol Measur*. 1977;1:385-401.
- 179. Lewis G, Pelosi AJ. The manual of CIS-R. London: Institute of Psychiatry; 1992.
- Olivares J, Garcia-Lopez LJ, Piqueras JA. Escala para la Detección de la Ansiedad Social (EDAS) [Social Anxiety Screening Scale, SASS]. In: Vera-Villaroel P, Oblitas L, eds. Manual de Escalas, & Cuestionarios Iberoamericanos en Psicología Clínica, & de la Salud [Handbook of Iberoamerican scales and tests in Health and Clinical Psychology]. Bogota, Colombia: Psicom Editores; 2005:350.
- Haavet OR, Sirpal MK, Haugen W, et al. Diagnosis of depressed young people in primary health care--a validation of HSCL-10. *Fam Pract*. 2011 Apr;28(2):233-7. doi: 10.1093/fampra/cmq078. PMID: 20937663.
- 182. Christensen KS, Fink P, Toft T, et al. A brief case-finding questionnaire for common mental disorders: the CMDQ. *Fam Pract*. 2005 Aug;22(4):448-57. doi: 10.1093/fampra/cmi025. PMID: 15814580.
- 183. Masia-Warner C, Storch EA, Pincus DB, et al. The Liebowitz social anxiety scale for children and adolescents: an initial psychometric investigation. *J Am Acad Child Adolesc Psychiatry*. 2003 Sep;42(9):1076-84. doi: 10.1097/01.CHI.0000070249.24125.89. PMID: 12960707.
- Richardson LP, McCauley E, Grossman DC, et al. Evaluation of the Patient Health Questionnaire-9 Item for detecting major depression among adolescents. *Pediatrics*. 2010 Dec;126(6):1117-23. doi: 10.1542/peds.2010-0852. PMID: 21041282.
- Birmaher B, Brent DA, Chiappetta L, et al. Psychometric properties of the Screen for Child Anxiety Related Emotional Disorders (SCARED): a replication study. *J Am Acad Child Adolesc Psychiatry*. 1999 Oct;38(10):1230-6. doi: 10.1097/00004583-199910000-00011. PMID: 10517055.
- 186. Monga S, Birmaher B, Chiappetta L, et al. Screen for Child Anxiety-Related Emotional Disorders (SCARED): convergent and divergent validity. *Depress Anxiety*. 2000;12(2):85-91. doi: 10.1002/1520-6394(2000)12:2<85::aid-da4>3.0.co;2-2. PMID: 11091931.
- Birmaher B, Khetarpal S, Brent D, et al. The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. *J Am Acad Child Adolesc Psychiatry*. 1997 Apr;36(4):545-53. doi: 10.1097/00004583-199704000-00018. PMID: 9100430.

- 188. La Greca AM, Stone WL. Social anxiety scale for children-revised: factor structure and concurrent validity. *J Clin Child Psychol*. 1993;22(1):17-27. doi: 10.1207/s15374424jccp2201 2
- 189. La Greca AM, Lopez N. Social anxiety among adolescents: linkages with peer relations and friendships. *J Abnorm Child Psychol*. 1998 Apr;26(2):83-94. doi: 10.1023/a:1022684520514. PMID: 9634131.
- 190. Puklek Levpuscek M. Lestvica Socialne Anksioznosti Za Mladostnike (LSAA). Prirocnik. Social anxiety scale for adolescents (SASA). Manual. Ljubljana, Slovenia: Center za psihodiagnosticna sredstva Psychological Test Publishing, Assessment and Consultancy; 2008.
- 191. Moore KA, Gee DL. The reliability, validity, discriminant and predictive properties of the Social Phobia Inventory (SoPhI). *Anxiety Stress Coping*. 2003;16:109–17.
- 192. Garcia-Lopez LJ, Hidalgo MD, Beidel DC, et al. Brief form of the Social Phobia and Anxiety Inventory (SPAI-B) for adolescents. *Eur J Psychol Assess*. 2008;24(3):150-6. doi: 10.1027/1015-5759.24.3.150.
- 193. Connor KM, Davidson JR, Churchill LE, et al. Psychometric properties of the Social Phobia Inventory (SPIN). New self-rating scale. *Br J Psychiatry*. 2000 Apr;176:379-86. doi: 10.1192/bjp.176.4.379. PMID: 10827888.
- 194. Connor KM, Kobak KA, Churchill LE, et al. Mini-SPIN: a brief screening assessment for generalized social anxiety disorder. *Depress Anxiety*. 2001;14(2):137-40. doi: 10.1002/da.1055. PMID: 11668666.
- 195. Seeley-Wait E, Abbott MJ, Rapee RM. Psychometric properties of the mini-social phobia inventory. *Prim Care Companion J Clin Psychiatry*. 2009;11(5):231-6. doi: 10.4088/PCC.07m00576. PMID: 19956461.
- 196. Spence SH. Social skills training: enhancing social competence with children and adolescents: Nfer-Nelson; 1995.
- 197. Topp CW, Østergaard SD, Søndergaard S, et al. The WHO-5 well-being index: a systematic review of the literature. *Psychother Psychosom*. 2015;84:167-76.
- 198. World Health Organization (WHO). Wellbeing measures in primary health care/The Depcare Project. Copenhagen: WHO Regional Office for Europe; 1998.
- 199. Cottrell DJ, Wright-Hughes A, Collinson M, et al. A pragmatic randomised controlled trial and economic evaluation of family therapy versus treatment as usual for young people seen after second or subsequent episodes of self-harm: the Self-Harm Intervention Family Therapy (SHIFT) trial. *Health Technol Assess*. 2018 Mar;22(12):1-222. doi: 10.3310/hta22120. PMID: 29532784.
- 200. Cottrell DJ, Wright-Hughes A, Eisler I, et al. Longer-term effectiveness of systemic family therapy compared with treatment as usual for young people after self-harm: an extended follow up of pragmatic randomised controlled trial. *EClinicalMedicine*. 2020 Jan;18:100246. doi: 10.1016/j.eclinm.2019.100246. PMID: 31956857.
- Mehlum L, Ramberg M, Tørmoen AJ, et al. Dialectical behavior therapy compared with enhanced usual care for adolescents with repeated suicidal and self-harming behavior: outcomes over a one-year follow-up. *J Am Acad Child Adolesc Psychiatry*. 2016 Apr;55(4):295-300. doi: 10.1016/j.jaac.2016.01.005. PMID: 27015720.
- 202. Mehlum L, Ramleth RK, Tørmoen AJ, et al. Long term effectiveness of dialectical behavior therapy versus enhanced usual care for adolescents with self-harming and

- suicidal behavior. *J Child Psychol Psychiatry*. 2019 Oct;60(10):1112-22. doi: 10.1111/jcpp.13077. PMID: 31127612.
- Haga E, Aas E, Grøholt B, et al. Cost-effectiveness of dialectical behaviour therapy vs. enhanced usual care in the treatment of adolescents with self-harm. *Child Adolesc Psychiatry Ment Health*. 2018;12:22. doi: 10.1186/s13034-018-0227-2. PMID: 29743941.
- 204. Ougrin D, Zundel T, Ng A, et al. Trial of therapeutic assessment in London: randomised controlled trial of therapeutic assessment versus standard psychosocial assessment in adolescents presenting with self-harm. *Arch Dis Child*. 2011 Feb;96(2):148-53. doi: 10.1136/adc.2010.188755. PMID: 21030367.
- Albano AM, Comer JS, Compton SN, et al. Secondary outcomes from the child/adolescent anxiety multimodal study: implications for clinical practice. *Evid Based Pract Child Adolesc Ment Health*. 2018;3(1):30-41. doi: 10.1080/23794925.2017.1399485. PMID: 30906874.
- 206. Taylor JH, Lebowitz ER, Jakubovski E, et al. Monotherapy insufficient in severe anxiety? Predictors and moderators in the child/adolescent anxiety multimodal study. *J Clin Child Adolesc Psychol*. 2018 Mar-Apr;47(2):266-81. doi: 10.1080/15374416.2017.1371028. PMID: 28956620.
- 207. Compton SN, Peris TS, Almirall D, et al. Predictors and moderators of treatment response in childhood anxiety disorders: results from the CAMS trial. *J Consult Clin Psychol*. 2014 Apr;82(2):212-24. doi: 10.1037/a0035458. PMID: 24417601.
- 208. Sanchez AL, Comer JS, Coxe S, et al. The effects of youth anxiety treatment on school impairment: differential outcomes across CBT, sertraline, and their combination. *Child Psychiatry Hum Dev.* 2019 Dec;50(6):940-9. doi: 10.1007/s10578-019-00896-3. PMID: 31087216.
- 209. Rynn MA, Walkup JT, Compton SN, et al. Child/adolescent anxiety multimodal study: evaluating safety. *J Am Acad Child Adolesc Psychiatry*. 2015 Mar;54(3):180-90. doi: 10.1016/j.jaac.2014.12.015. PMID: 25721183.
- 210. Gordon-Hollingsworth AT, Becker EM, Ginsburg GS, et al. Anxiety disorders in Caucasian and African American children: a comparison of clinical characteristics, treatment process variables, and treatment outcomes. *Child Psychiatry Hum Dev*. 2015;46(5):643-55. doi: 10.1007/s10578-014-0507-x. PMID: 2014-43106-001.
- Ginsburg GS, Kendall PC, Sakolsky D, et al. Remission after acute treatment in children and adolescents with anxiety disorders: findings from the CAMS. *J Consult Clin Psychol*. 2011 Dec;79(6):806-13. doi: 10.1037/a0025933. PMID: 22122292.
- Osimo EF, Stochl J, Zammit S, et al. Longitudinal population subgroups of CRP and risk of depression in the ALSPAC birth cohort. *Compr Psychiatry*. 2020;96:152143. doi: 10.1016/j.comppsych.2019.152143. PMID: 2020-00258-001.
- 213. Walkup JT, Labellarte MJ, Riddle MA, et al. Searching for moderators and mediators of pharmacological treatment effects in children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2003 Jan;42(1):13-21. doi: 10.1097/00004583-200301000-00006. PMID: 12500072.
- Ginsburg GS, Riddle MA, Davies M. Somatic symptoms in children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry*. 2006 Oct;45(10):1179-87. doi: 10.1097/01.chi.0000231974.43966.6e. PMID: 17003663.

- 215. Reinblatt SP, dosReis S, Walkup JT, et al. Activation adverse events induced by the selective serotonin reuptake inhibitor fluvoxamine in children and adolescents. *J Child Adolesc Psychopharmacol*. 2009;19(2):119-26. doi: 10.1089/cap.2008.040. PMID: 2009-05505-003.
- 216. Caporino NE, Read KL, Shiffrin N, et al. Sleep-related problems and the effects of anxiety treatment in children and adolescents. *J Clin Child Adolesc Psychol*. 2017 Sep-Oct;46(5):675-85. doi: 10.1080/15374416.2015.1063429. PMID: 26467211.
- 217. Curry J, Rohde P, Simons A, et al. Predictors and moderators of acute outcome in the Treatment for Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1427-39. doi: 10.1097/01.chi.0000240838.78984.e2. PMID: 17135988.
- Emslie G, Kratochvil C, Vitiello B, et al. Treatment for Adolescents with Depression Study (TADS): safety results. *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1440-55. doi: 10.1097/01.chi.0000240840.63737.1d. PMID: 17135989.
- 219. Kennard B, Silva S, Vitiello B, et al. Remission and residual symptoms after short-term treatment in the Treatment of Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1404-11. doi: 10.1097/01.chi.0000242228.75516.21. PMID: 17135985.
- Vitiello B, Rohde P, Silva S, et al. Functioning and quality of life in the Treatment for Adolescents with Depression Study (TADS). *J Am Acad Child Adolesc Psychiatry*. 2006 Dec;45(12):1419-26. doi: 10.1097/01.chi.0000242229.52646.6e. PMID: 17135987.
- 221. Sparse whole-genome sequencing identifies two loci for major depressive disorder. *Nature*. 2015 Jul 30;523(7562):588-91. doi: 10.1038/nature14659. PMID: 26176920.
- 222. Reynolds WM. 5.17 Depression. *Comprehensive Clinical Psychology*. 1998;5:419-61. doi: 10.1016/B0080-4270(73)00135-8.
- 223. Kuo ES, Stoep AV, Stewart DG. Using the short mood and feelings questionnaire to detect depression in detained adolescents. *Assessment*. 2005 Dec;12(4):374-83. doi: 10.1177/1073191105279984. PMID: 16244118.
- Wood A, Kroll L, Moore A, et al. Properties of the mood and feelings questionnaire in adolescent psychiatric outpatients: a research note. *J Child Psychol Psychiatry*. 1995 Feb;36(2):327-34. doi: 10.1111/j.1469-7610.1995.tb01828.x. PMID: 7759594.
- 225. Birleson P. The validity of depressive disorder in childhood and the development of a self-rating scale: a research report. *J Child Psychol Psychiatry*. 1981 Jan;22(1):73-88. doi: 10.1111/j.1469-7610.1981.tb00533.x. PMID: 7451588.
- 226. Hamilton A. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.
- 227. Findling RL, Robb A, Bose A. Escitalopram in the treatment of adolescent depression: a randomized, double-blind, placebo-controlled extension trial. *J Child Adolesc Psychopharmacol*. 2013 Sep;23(7):468-80. doi: 10.1089/cap.2012.0023. PMID: 24041408.
- 228. McGlinchey EL, Reyes-Portillo JA, Turner JB, et al. Innovations in practice: The relationship betweensleep disturbances, depression, and interpersonal functioning in treatment for adolescent depression. *Child Adolesc Ment Health*. 2017 May;22(2):96-9. doi: 10.1111/camh.12176. PMID: 28947892.

229.	Brent DA, Porta G, Rozenman MS, et al. Brief behavioral therapy for pediatric anxiety and depression in primary care: a follow-up. <i>J Am Acad Child Adolesc Psychiatry</i> . 2019 Jul 3doi: 10.1016/j.jaac.2019.06.009. PMID: 31278996.